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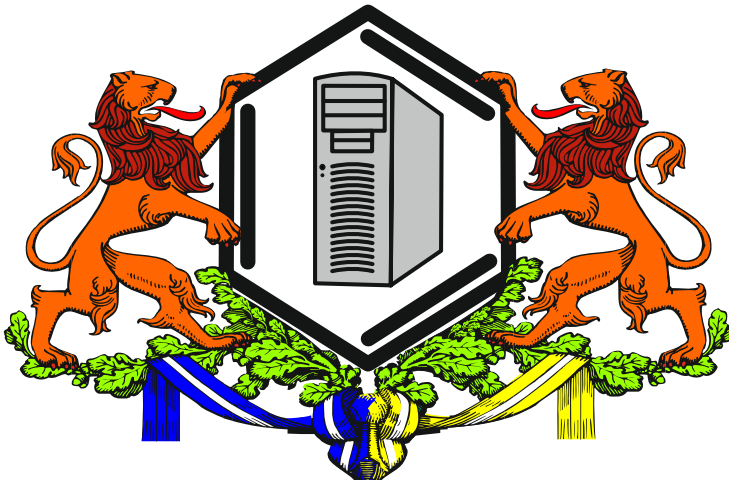

BOOK OF ABSTRACTS

Methods and Applications of Computational Chemistry

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Methods and Applications of Computational Chemistry

4th International Symposium

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Local hybrids: a new generation of exchange-correlation functionals for the description of a wide range of properties

Alexei V. Arbuznikov, Hilke Bahmann, Kolja Theilacker, and Martin Kaupp

Institute of Chemistry, Technical University of Berlin, Straße des 17. Juni 135, D-10623 Berlin, Germany; E-mail: alexey.arbuznikov@tu-berlin.de

The accuracy of Kohn-Sham density functional calculations is known to be governed by the quality of underlying exchange-correlation functionals. Among the latter, a particular place is occupied by very popular nowadays highly accurate "global hybrid functionals" (like B3LYP, PBE0 or TPSSh) that include a certain percentage of the exact exchange. However, their performance is restricted by insufficient flexibility, since the description of different properties requires very different amounts of exact exchange. The flexibility is fundamentally enhanced by passing to a position-dependent exact-exchange admixture governed by a so-called local mixing function (LMF) that leads to the notion of local hybrid functionals. The latter constitute a new promising generation of hyper-GGA functionals for the simultaneous accurate description of various molecular properties within Kohn-Sham DFT.

The overall performance of local hybrids is a matter of a very subtle balance between their basic ingredients: (i) *ansatz* and parameterization of the LMF; (ii) density-functional approximation of the exchange mixed with the exact exchange; (iii) nature of the (dynamic) correlation functional. Up to now, the best performance has been attained partially in a semi-empirical way with a scaled ratio of von Weizsäcker kinetic energy density to local kinetic energy density as LMF [1] (the latter may also include spin polarization [2]), LSDA exchange, and LSDA correlation. Further progress can be aided by insights from the adiabatic connection (AC) formalism [3] and careful analysis of exact constraints (Lieb-Oxford bound, density-scaling properties, etc.) a density functional should obey.

Our best local hybrids include a minimal number of adjustable parameters (one or two) and turn out to be superior in the description of atomization energies, reaction barrier heights [1,2,4], NMR chemical shifts [5], EPR g tensors [6], and electric response properties (polarizabilities and hyperpolarizabilities) [7] compared to traditional hybrids that often suffer from being overparameterized. Recently we have supplemented our local hybrids with Grimme's DFT-D3 additive semi-empirical dispersion corrections: the resulting scheme provides a very good description of weak noncovalent interactions [8].

Implementation aspects (enhancement of the computational efficiency in the evaluation of LMF-including two-electron integrals) and an outlook on the extension of local hybrids to computation of other properties are discussed as well.

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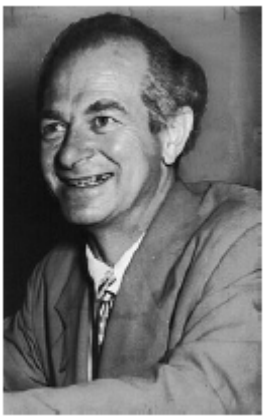
Valence Bond type analysis of (Frozen) Molecular Orbital based calculations

Xavier Assfeld

Equipe de Chimie et Biochimie Théoriqu, BP 70239, 54506 Vandoeuvre;France; E-mail: Xavier.Assfeld@cbt.uhp-nancy.fr

Two competitive methods can be considered as the cornerstones of Quantum Chemistry, namely the Valence Bond (VB) approach, mainly divulgated by Pauling, and the Molecular Orbital (MO) one, mainly founded by Mulliken.



Linus Pauling (1901-1994)

Robert Mulliken (1896-1986)

On one hand, Pauling's description of a chemical bond implies the interaction of three configurations: one covalent, where two electrons are shared equally between the two atoms; two ionic configurations, where the two electrons belong either to one atom or to the other. The Valence Bond theory uses this definition to perform quantum chemical calculations. However, due to the cost of such calculations, this method is generally devoted to systems containing less than 50 electrons.

On the other hand, MO theory can be used for large systems with more than one hundred atoms, but, as it mixes intimately the three above mentioned configurations, one looses the elegant interpretative Pauling's analysis.

During this lecture, I will present a tool able to extract the configurations, their respective energies and their interactions, from calculations based on Frozen Molecular Orbitals [1]. Application to the ortho effect of fluorine atom on the metal-aryl bond will be presented.

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Atomistic Multiscale Simulation of Nanostructured Materials for Photonic Applications

Alexander Bagaturyants, Michael Alfimov

Photochemistry Center, Russian Academy of Sciences, ul. Novatorov 7a, b. 1, Moscow 119421 Russia

Hierarchically constructed nanostructured materials, in which the structure of a lower level of scale is built into the structure of a higher level of scale, attract particular interest. The development of nanostructured materials for optical chemical gas sensors is an example of this application. The functionality of such a material is provided by a photoactive molecule (indicator molecule, IM) such that it strongly changes its optical response (mostly, luminescence) upon interaction with a target molecule (detected or analyte molecule, AM). IM represents the lowest level of the hierarchy and is built into a local structure forming a receptor center (RC), which in its turn is built into a nanoparticle (NP).

The goal of simulation in this case is to predict the optical properties of the entire structure (sensing material) and its response to various AMs. A methodology is developed for the predictive multiscale simulation of the structure and properties of hierarchical organic nanomaterials for nanophotonics based on the consistent use of atomistic methods. In the case of optical chemosensors, the use of atomistic simulation methods is restricted to the first three levels: IM, RC, and NP.

The possibilities of modern atomistic simulation methods are considered using specific examples. It is shown that multiscale atomistic simulation at the modern theoretical level allows the main functional properties of materials for micro- and nanoelectronics and photonics to be described and predicted with adequate reliability [1–10].

The authors are grateful to all the coauthors of the cited papers for useful discussions and numerous calculated results. The work was supported by the Presidium and the Branch of General and Technical Chemistry of the Russian Academy of Science, the Ministry of Education and Science, and the Russian Foundation for Basic Research.

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The implicit electrostatic solvent model with continuous dielectric permittivity function

Mikhail V. Basilevsky[a], Fedor V. Grigoriev[a], Ekaterina A. Nikitina[a], Jerzy Leszczynski[b]

[a] *Photochemistry Center, Russian Academy of Sciences, Moscow, Russia*
[b] *Jackson State University, Jackson MS, USA*

The modification of the electrostatic continuum solvent model considered in the present work is based on the exact solution of the Poisson equation, which can be constructed provided the dielectric permittivity ε of the total solute and solvent system is an isotropic and continuous spatial function. This assumption allows one to formulate a numerically efficient and universal computational scheme which covers the important case of variable ε function inherent to the solvent region. The obtained type of solution is unavailable for conventional dielectric continuum models such as Onsager and Kirkwood models for spherical cavities and the polarizable continuum model (PCM) for solute cavities of general shape which imply that ε is discontinuous on the boundary confining the excluded volume cavity of the solute particle. Test computations based on the present algorithm are performed for water and several non-aqueous solvents. They illustrate specific features of this approach, called "smooth boundary continuum model" (SBCM), as compared to the PCM procedure, and suggest primary tentative results of its parameterization for different solvents. The calculation for the case of a binary solvent mixture with variable ε in the solvent space region demonstrates the applicability of this approach to a novel application field covered by the SBCM. Some methodological problems, arising when the present computational algorithm is compared with the classical dielectric continuum models, will be discussed.

The Use of Continuous Molecular Fields and Quantum Similarity Measures in SAR/QSAR/QSPR Studies and Drug Design

I. I. Baskin [a], P. V. Carpov [a], N. I. Zhokhova [a], N. S. Zefirov [a]

[a] *Department of Chemistry, Moscow State University, Moscow, Russia*

We present a new methodology for building classification Structure-Activity Relationships (SAR), regression Quantitative Structure-Activity Relationships (QSAR) and Quantitative Structure-Property Relationships (QSPR) models based on joint application of modern kernel-based statistical learning methods [1] with description of chemical objects by means of continuous functions, such as various types of molecular fields (electrostatic, steric, hydrophobic, etc) and the function of electron density. In this presentation, we show the ways how molecular fields can be encapsulated into kernels and through this universal mechanism be used to build QSAR (see preliminary communication [2]) and QSPR regression models; 2-class classification SAR models, perform ligand-based virtual screening based on similarity of molecular fields using 1-class classification (novelty detection) mechanism, analyze and visualize continuous fields of model parameters (regression coefficients or direction cosines of the vector perpendicular to separating hyperplane in the corresponding function Hilbert space), etc. The prospects for using the afore-mentioned visualization technique in drug design are discussed.

The second part of the presentation deals with the use of Molecular Quantum Similarity measures (developed earlier by R. Carbó-Dorca et al [3]) for encapsulating electron density functions into kernels suitable for being used in conjunction with kernel-based statistical learning methods. The electron density functions needed for this purpose can be either computed using quantum chemistry methods or efficiently approximated by means of additive approaches. Several examples of kernel-based statistical models built using the electron density functions of molecules are discussed. Very close integration of chemoinformatics and quantum chemistry approaches offered by this methodology is believed to be beneficial for further development of computational chemistry.

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Gas-phase spectroscopy of biomolecules and *ab initio* simulations

V. Brenner

Laboratoire Francis Perrin, CEA-CNRS URA 2453, DSM/IRAMIS/SPAM, CEA-CE Saclay, Bat 522, Gif sur Yvette Cedex, F-91191 FRANCE

The gas-phase studies of biomolecules, building blocks of proteins, play a central role in the understanding of structure and dynamics of such more complex systems. Studies on peptides for example providing useful reference data offer access to important topics like protein folding, H-bonding networks and cooperative effects or protein first solvation shell. Success of such studies requires however interplay between experiment and theory in order to allows advances in the understanding of such problems. One of the goals for theory is to guide from benchmarking of quantum chemistry techniques on short peptide chains the choice of efficient ab initio methods by comparison with spectroscopic data. In this context, key points for the theory concern structure and energetics of these systems as well as the vibrational molecular spectroscopy. Today, the electronic structure of small molecular systems can be treated with very high accuracy and even the electronic structure of very large molecular systems can often be treated with sufficient accuracy. However, the vibrational structure theory applied is often based on the harmonic approximation, even if molecular systems such as small peptides are not particularly rigid and present anharmonicity vibrational motion which can be important. After a brief discussion on the available and applicable methodologies to go beyond the harmonic approximation in such systems, one or two for examples of studies on small peptides using both gas-phase laser spectroscopy and quantum chemistry will be presented and discussed.

The thermodynamic and Kinetic Description of the Reactions of the Organometallic Complexes

Jaroslav V. Burda

Department of Chemical Physics and Optics, Charles University in Prague, 121 16 Prague 2,Czech Republic

The interaction of the derivatives of cisplatin (diammine-dichloro-platinum(II) complex) with amino acids were explored in various environment. Similarly, the hydration process of cisplatin was re-considered. compared with an aquation reaction, which can be considered as an activation of these metallodrugs.

Detailed mechanism of the adduct formation of diaqua-tetrakis-μ-acetatodirhodium to purine DNA bases is examined using ammonia and guanine as a model for interacting species (nucleobase), which attacks the Rh-O(acetyl) or Rh-O(aqua) coordination bonds. Several different mechanisms were explored modeling different environment of the complex. Thermodynamic affinity and as well as kinetic data for the ammonia interaction with Rh-complex demonstrate presence of a enhanced reaction mechanismin acidic environment.

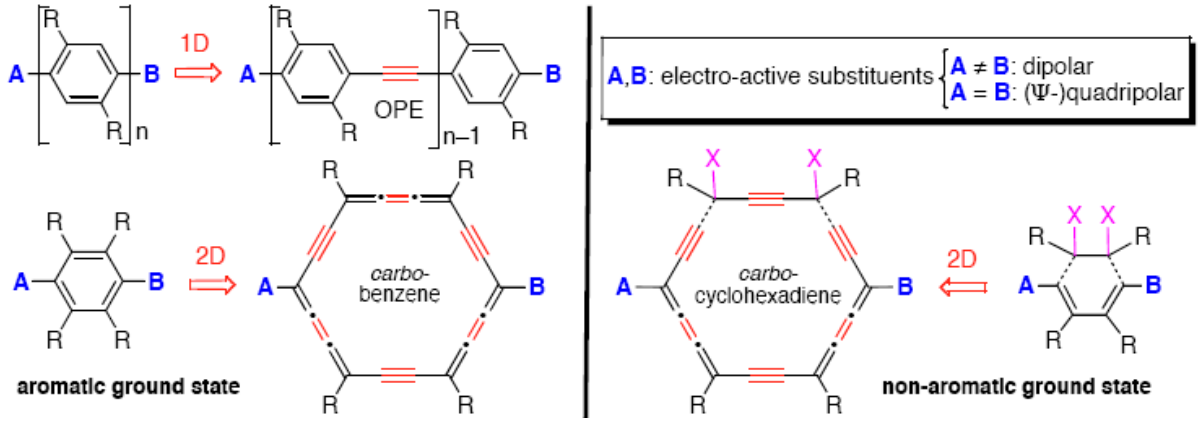
Comparison of different ruthenium complexes in the process of activation was performed. Replacement of the chloro-ligand in $[Ru(II)(Arene)(en)Cl]^+$ and $[Ru(II)(Arene)(PTA)Cl_2$ was examined together with cisplatin “reference” complex. Obtained results clearly demonstrate correlation between bond strength of the Ru-Cl coordination and reaction barrier of the metallocomplex.

Influence of dimensionality, polarity, and aromaticity on spectroscopical and optical properties of carbo-chromophores

Christine Lepetit, Remi Chauvin

Laboratoire de Chimie de Coordination of the CNRS, Paul Sabatier University, 205 Route de Narbonne, 31077 Toulouse cedex 4, France; E-mail :chauvin@lcc-toulouse.fr

Highly π-conjugated multipolar organics are promising chromophores for molecular materials with linear or non-linear optical (NLO) properties required for various applications. The nature and extent of the bridge between electro-active ends prove to be crucial, but most of the efficient chromophores are based on oligomethyne scaffolds ($[sp^2\text{-CH}]_n$) with various topologies, including more or less aromatic cyclic motifs which effects have been theoretically analyzed [1]. Insertion of dicarbon rods ($[sp\text{-C}]_2$) expands the size of the scaffold, while preserving the topology and not disrupting the π-conjugation (*carbo*-mer principle) [2]. The dimensionality of the insertion can be partial (e.g. 1D-expansion along the axis between the electroactive ends), or complete (2D-expansion of the bridge). Whereas oligophenylethynylenes (OPEs) can thus be regarded as linear *carbo*-mers of the corresponding oligo-*p*-phenylenes [1], *carbo*-benzenes are ring *carbo*-mers of the benzenic parents [2]. The aromatic character of *carbo*-benzenes has been demonstrated by many theoretical methods and criteria (topological, energetic, geometric, electronic, magnetic) [1,3]. Disruption of the conjugation in the corresponding carbocyclohexadiene ring allows to appraise the effect of ground state aromaticity on the properties of these *carbo*-chromophores [3]. Their ground and first excited states were investigated at the semiempirical or TD-DFT level, and correlated with particular chromophoric properties such as 2nd order NLO properties, two-photon absorption properties, dichromism [1,3-5]... The substituent effects (R = OCH_3, Ph, CF_3) have also been investigated [6].



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A Detailed Analysis of QSPR Modeling

Tim Clark

Computer-Chemie-Centrum der Friedrich-Alexander Universität Erlangen-Nürnberg, Nägelsbachstrasse 25, 91052 Erlangen, Germany, and

Centre for Molecular Design, University of Portsmouth, Mercantile House, Portsmouth PO1 2EG, UK

The performance-limiting factor in QSPR models is usually not the computational techniques used to construct the model, but rather the quantity and quality of the experimental data [1]. One property for which the data situation is better than usual is the water-octanol partition coefficient, expressed as $\log P_{OW}$. We have therefore investigated modeling this quantity in detail using binned surface-integral models [2]. The quantity and the quality of the data allow us to investigate factors such as the effect of molecular conformation or the extent of the applicability domain on the performance of the models.

The results of this work will be described along with other analyses of QSPR models. In particular, the use of the binned surface-integral functions as local hydrophibicities and their relationship, for instance to scoring functions will be discussed.

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Calculated Vertical Ionization Energies of the Common α-Amino Acids in the Gas Phase and in Solution

David M. Close

Department of Physics, Box 70652, East Tennessee State University, Johnson City, TN, 37614 USA

The vertical ionization energies of the low lying conformers of the α-amino acids found in proteins have been calculated. Geometry optimizations were first performed at the B3LYP/6-311G(d,p) level of theory, and then reoptimized at the MP2/6-311G(d,p) level of theory. Vertical ionization energies were then computed by three methods, electron propagator in the partial third order (P3) approximation, Outer-Valence-Green's Functions, and by evaluating the difference in the total energy between the cation radical and the neutral amino acid in the geometry of the neutral species. When available, the results are compared with the experimental vertical ionization energies. The vertical ionization energies calculated using the MP2/P3 method gave the best overall agreement with the experimental results. Next the ionization energies in solution are calculated for the zwitterionic forms of the α-amino acids by using IEPCM methods. To obtain the vertical ionization energy in solution it is necessary to use the nonequilibrium polarizable continuum model (NEPCM) the results of which are reported here for the α-amino acids.

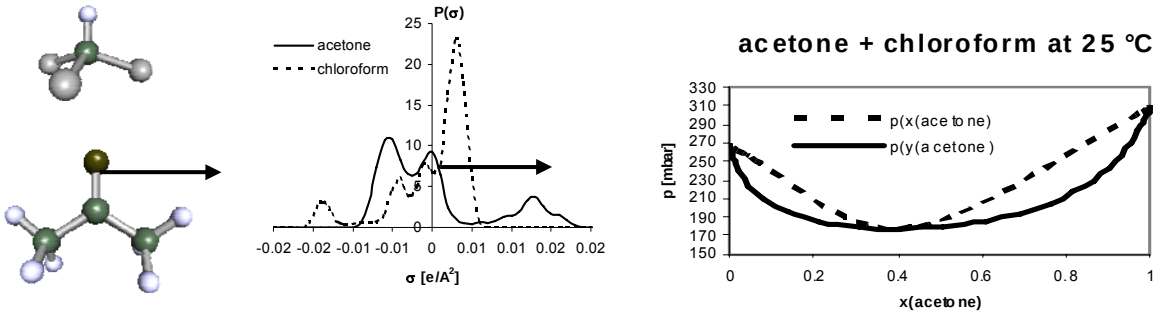
To study amino acids in peptides, calculations were performed with density functional theory. B3LYP/6-311G(d,p) calculations gave poor results of the vertical ionization energies, while the use of the M05-2X functional gave rather good results. New calculations will be presented on adiabatic ionization energies of the amino acids, along with a discussion of the types of fragmentation (loss of COOH, loss of the side chain, no fragmentation, but perhaps significant reorganization in forming the radical cation).

From DFT to Liquid Phase Thermodynamics and Back

M. Diedenhofen, A. Klamt

COSMOlogic GmbH & Co.KB, Leverkusen, Germany

During the last decade the quantum chemically based COSMO-RS [1] (COSMO for realistic solvation) method has become a widely accepted method in the fields of chemical engineering and physical chemistry. A schematic work flow of the entire procedure is given below. In the first step DFT calculations, employing the conductor-like continuum solvation model (COSMO) [2], are performed. The results of this calculations i.e. the energies and the apparent surface charge density (σ) of the continuum model, are used in the subsequent COSMO-RS step. COSMO-RS is a statistical thermodynamics model using σ-based surface interactions. From this calculation we receive the chemical potential of all compounds of a mixture at a given temperature and composition. This key-value can be used for the prediction of a variety of thermodynamic equilibrium properties, e.g the vapor-liquid equilibrium shown in the figure below.



The talk will present an overview of the current theory and illustrate the way from DFT to fluid phase property prediction. Examples from different fields of applications will be given, especially the property prediction of ionic liquid (IL) mixtures. At the end the Direct COSMO-RS theory, which uses the COSMO-RS potential in SCF calculations, will be presented.

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Magnetic effects in finite single-walled carbon nanotubes from first principles.

Frank Hagelberg[a] and Jianhua Wu[b]

[a]*Department of Physics and Astronomy, East Tennessee State University, Johnson City, TN 37614, USA*

[b]*Department of Physics, Atmospheric Sciences, and Geoscience, Jackson State University, Jackson, MS 39217, USA*

Previous computational research on single-walled carbon nanotubes (SWCNTs) of the zigzag type has mostly dealt with infinite periodic tubes. Reducing a zigzag tube to finite length gives rise to SWCNT ground state magnetism [1]. This contribution deals with the impact of various structural and environmental tube parameters on the magnetism of the system, among them curvature, topological defects as well as metal atom impurities.

Inspecting the behavior of the magnetic moment with the diameter of the zigzag tube by plane-wave density functional theory (DFT) simulation, an oscillatory increase is observed for a large set of systems, with indices ranging from 7 to 21. Whenever the tube index is a multiple of 3, the tube turns metallic in the periodic limit, and a linear increase of the magnetic moment is found. This is the signature of a universal magnetic relation between a metallic zigzag nanotube and its planar twin, a zigzag graphene nanoribbon. As the tube is flattened, its magnetic moment increases consistently by two atomic units, irrespective of its diameter.

To make contact with experiment, one has to include SWCNTs with structural irregularities. In particular, Stone-Wales defects are known to be ubiquitous features of the nanotube surface, and to alter the energetic and electronic properties of SWCNTs. The question followed here by investigation of several zigzag SWCNT prototypes (for two examples, see Figure 1) is if these defects modify the magnetic structure of the finite tube. As suggested by the computational results obtained so far, the magnetic moment is resistant with respect to inclusion of Stone-Wales impurities. Thus, the magnetism of a zigzag nanotube reacts sensitively to changes of the tube dimension, as well as to the nature and number of external adsorbates [2], but remains unaffected by the presence of topological defects. The calculated conductivity, however, turned out to respond markedly to the presence of Stone-Wales impurities. As a function of the bias, the conductivity was shown to display periodic behavior for pure SWCNTs. Modifying the SWCNT structure by introduction of defects turned out to destroy the periodicity.

Further, insertion of transition metal atom impurities as a technique to tailor both the magnetic structure and the conductivity of the tube [3] will be discussed. The relevance of SWCNT magnetism studies for understanding fundamental nanotube properties and for establishing these systems as candidates for novel spin-based nanodevices will be emphasized.

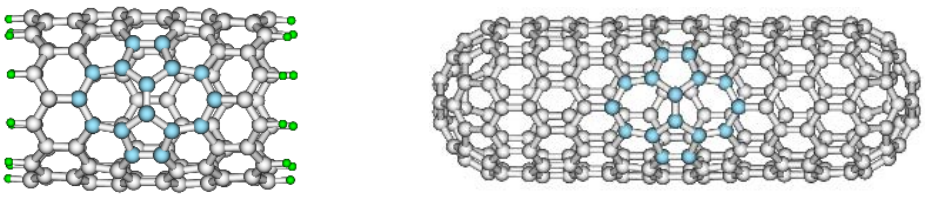

Figure 1. Hydrogen-terminated (left) and capped SWCNT (right) with Stone-Wales defect.

[1] J.Wu, F.Hagelberg, Magnetism in finite-sized single walled carbon nanotubes of the zigzag type, Phys. Rev. B 79, 115436 (2009)

[2] J.Wu, F. Hagelberg, Adsorption of small hydrocarbon radicals on single walled carbon nanotubes of finite length, Phys.Rev.B 81 155407 (2010)

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Alkaline hydrolysis of nitroaromatic compounds: M06-2x DFT study

Frances C. Hill,[a] Liudmyla Sviatenko,[b,c] Leonid Gorb,[d] Sergiy I. Okovytyy,[b,e] and Jerzy Leszczynski[a,b]

[a]*US Army ERDC, Vicksburg, MS 39180*

[b]*Interdisciplinary Center for Nanotoxicity, Department of Chemistry and Biochemistry, Jackson State University, Jackson, Mississippi 39217, USA*

[c]*Kirovograd State Pedagogical University, Kirovograd, 25006, Ukraine;*

[d]*Badger Technical Services, LLC, Vicksburg, Mississippi, USA;*

[e]*Department of Organic Chemistry, Dnipropetrovsk National Univesity*

TNT, DNT and DNAN are environmental contaminants and understanding their environmental fate is an important task. A very promising method to alter these nitrocompounds and perhaps reduce their environmental impact is alkaline hydrolysis. The mechanism of this reaction was investigated computationally along with simulation of UV-VIS and NMR spectra.

All the calculations were performed with the Gaussian 09 suite of programs. All relevant stationary points (intermediates, transition states, and products) were fully optimized at the SMD(Pauling)/M06-2X/6-31+G(d,p) level. Stationary points were further characterized as minima having all real frequencies, or as transition states possessing only one imaginary frequency, by computing analytic harmonic vibrational frequencies at the same theory level as geometry optimization.

Because available experimental data had been generated at room temperature or higher, the best characteristic to take into account the influence of temperature is the change of Gibbs free energy that actually govern a chemical reaction. Therefore, we calculated those values for each reaction as

$$\Delta G = \Delta H - T\Delta S$$

and the change of Gibbs activation energy as

$$\Delta G^{\approx} = \Delta H^{\approx} - T\Delta S^{\approx}$$

where ΔG, ΔH and ΔS are the change of the Gibbs free energy, enthalpy and entropy respectively and the subscript "≈" relates to transition state.

UV-VIS-spectra of initial compounds, intermediates and products of the alkaline hydrolysis of TNT, DNT and DNAN were calculated at the SMD(Pauling)/M06-2X/6-31+G(d,p) level.

The results obtained are validated by available experimental data on the alkaline hydrolysis of TNT and suggest the formation of Meisenheimer complexes and an anion of TNT as first-step intermediates. We have found that the reaction proceeds though polynegative complexes followed by aromatic ring-opening and breaking of the carbon chain. Another possible pathway that was determined computationally leads to polymeric products through Janovsky complex formation. Our final results suggest that DNT and DNAN will be more resistant to alkaline hydrolysis as compared to TNT.

First principles molecular dynamics investigations of Si-based nanolayered systems

V. I. Ivashchenko[a], P. E. A. Turchi[b], P.L. Skrynskyy[a], O.K. Porada[a]

[a]*Institute of Problems of Material Science, NAS of Ukraine, Krzhyzhanosky str. 3, 03142 Kyiv, Ukraine*

[b]*Lawrence Livermore National Laboratory (L-352), P.O. Box 808, Livermore, CA 94551, USA*

Empirical potential molecular dynamics simulations and first-principles total-energy calculations were carried out to investigate possible structural transformations in nano-layered (111) twin silicon systems under uni-axial compression. It was established that uni-axial compression of the twinned silicon structures causes the formation of the segments with the five-fold coordinated orthorhombic structure (space group Fmmm) at ~ 25 GPa. Such a structural transformation occurs only for the twin nanolayered structures with layer thickness not exceeding ~ 3 nm. This transformation is a first-order phase transition, and the new structure is characterized by an increase of the failure stress above 37 GPa. The orthorhombic phase transforms into the tetragonal one (space group I4/mmm) after decompression at 300 K. The unit cells of the compressed and decompressed segment structures are shown in Fig. 1. In Fig. 2 we show the total energy and enthalpy of the Fd-3m and I4/mmm phases as functions of cell volume and pressure, respectively. First-principles pseudo-potential calculations confirm the formation of the tetragonal phase and show that both the orthorhombic and tetragonal phases will exhibit a metallic character. Finally, this study clearly showed that phase transformations in a single crystal and its twin structures could occur along different paths.

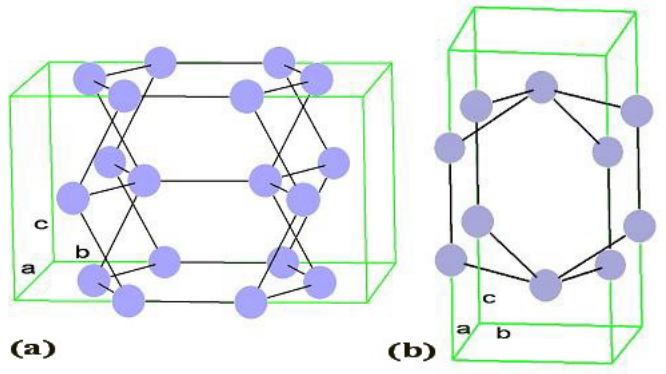


Figure 1. Unit cells of the primitive orthorhombic (space group Fmmm) (a) and tetragonal (space group I4/mmm) (b) lattices.

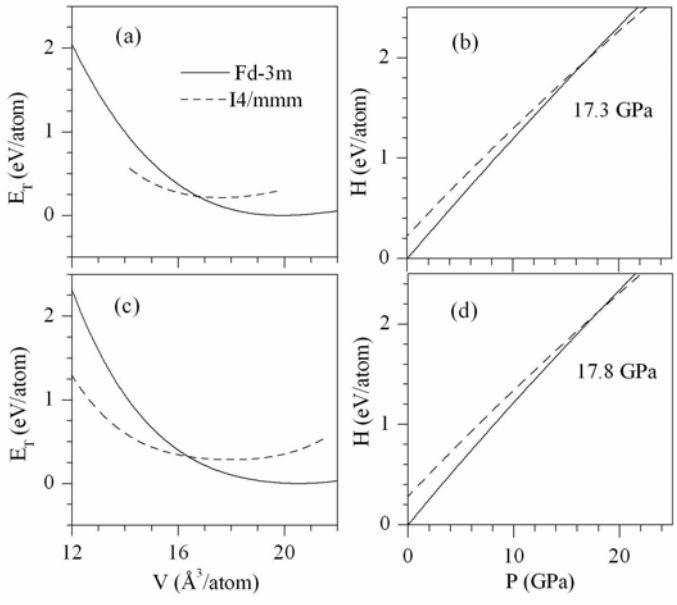


Figure 2. Cohesive (E_{COH}) and total (E_T) energies – cell volume (V) and enthalpy (H) – pressure (P) dependencies for the Fd-3m and I/4mmm structures calculated by using the Tersoff approach (a,b) and the first-principles pseudo-potential method (c,d). The numerals indicate the transition pressures.

Solvent effects and solvent parameters

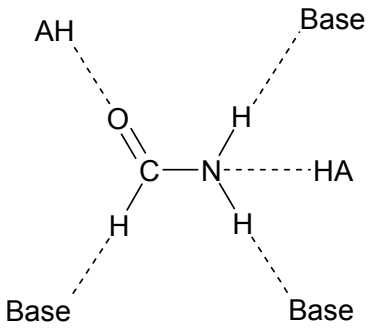
T.M. Krygowski,[a] H. Szatyłowicz[b]

[a]***Department of Chemistry, Warsaw University, Pasteura 1, 02-093 Warsaw; e-mail: tmkryg@chem.uw.edu.pl***

[b]***Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw***

Solvent effects on chemical and biochemical processes as well as on physicochemical properties have been subject of huge amount of works, which are nicely reviewed in excellent monograph by Reichardt [1]. The idea of amphotheric properties of aprotic solvents considered in terms of Lewis acid/base theory was presented in mid 70-ties [2] and is also associated with the Kamlet and Taft approach to the solvent effect in which solvents are classified into: solvent H-bond acceptor basicities (HBA) [3] and H-bond donor acidities (HBD). [4]

In terms of solvent parameters formamide is a Lewis base of medium strength, its Kamlet-Taft β value is 0.40, and as a Lewis acid has Reichardts $E_T = 0.775$, both quantities in a 0.0 – 1.0 scale. In other words, formamide is more acidic than basic in terms of Lewis definition of acids and bases. The H-bond formation is possible for each non-carbon atoms of formamide.



The dots show potential localization of H-bonding

Application of the method based on the approaching of either the base (e.g. F^-) or acid (e.g. HF) [5]to the appropriate Lewis acidic or basic centers, respectively, allows to estimate numerically their power (in acidity or basicity) by analyzing characteristics of the H-bonding formed. Computation for the above presented modeling is carried out at the B3LYP/6-311++G** level.

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[3] M.J. Kamlet, R.W. Taft, *J. Am. Chem. Soc*. **98** (1976) 377–383.

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Proton transfer dynamics in strong intramolecular hydrogen bonded systems

Zdzisław Latajka

Faculty of Chemistry, University of Wrocław, F.Joliot-Curie 14, 50-383 Wrocław, Poland

Proton transfer in hydrogen bonds is one of the most important phenomenons influencing dynamical behavior in many chemical and biological systems. In many living systems very fast proton transfer processes occur and moreover in many cases a proton behaves as a quantum particle tunneling through the energy barrier. Despite widespread importance of tunneling effects, the quantum character of proton transfer is not frequently use in theoretical models or is restricted only to the zero-temperature quantum effects in simple model systems with severe reduced dimensionality of considered systems.

The rapid development of computer power with efficient codes as well as theoretical models gives us an opportunity to study the dynamics of proton transfer processes with a great accuracy. However, the classical Molecular Dynamics with the potential derived from Molecular Mechanics (Force Fields) is not able to take into account large electron distribution accompanying the transfer of proton from one subunit to another. The Car-Parrinello Molecular Dynamics (CPMD) is very efficient scheme for description of dynamics of molecular systems. In contrary to the classical molecular dynamics the CPMD calculations do not require an a priori determined model interaction potential because the internuclear forces for each configuration of nuclei are calculated from the first principle – the model Hamiltonian is defined in the Density Functional Theory formalism. The quantum behavior of proton from a hydrogen bridge as well as remaining heavy atoms can be taken be means of the Path Integration Molecular Dynamics (PIMD).

The chemical systems with strong single or double O-H…O hydrogen bonds are very common in many chemical and biological systems. In the lecture results of CPMD and PIMD calculations will be presented for the examples of proton transfer in strong intramolecular O-H...O and N-H...N hydrogen bonds will be presented. The classical and quantum nature of bridged proton will be discussed.

Acknowledgements: Support from Ministry of Science and Higher Education of Polad (grant No. N N204 0958 33) is acknowledged. Calculations were performed at the Wrocław Centre for Networking and Supercomputing (WCSS) and the Academic Computer Centre in Gdańsk (CI TASK).

ELF analysis of the coordinating properties of strongly or poorly donating ligands

Christine Lepetit, Ibrahim Abdellah, Carine Maaliki, Yves Canac, Remi Chauvin

Laboratoire de Chimie de Coordination UPR 8241 CNRS, 205, Route de Narbonne, F-31077 Toulouse cedex 04-France; e-mail: christine.lepetit@lcc-toulouse.fr

Electron localization function (ELF) analysis is a versatile tool for the description of chemical bonding, especially in challenging situations such as multicentric bonds, donor-acceptor bonds, partly ionic or weakly covalent interactions, partial hapticity …. Recent illustrations extracted from the coordination chemistry of strongly donating carbon ligands such as phosphonium ylides and yldiides or poorly electron-donating amidiniophosphines will be discussed.

ELF analysis allows for the weighting of the most representative mesomeric forms of the « free » or coordinated ligand. Amidiniophosphines are described as diaminocarbene (NHC)→phosphenium adducts (Figure 1a) [1]. ELF Fukui indices point their dative C–P bond as the most reactive site towards nucleophiles in agreement with the experimental results. On the basis of ELF analysis, a η^2-P,C haptomeric form has been suggested to contribute significantly to the coordination mode of phosphonium ylide or yldiide ligands (Figure 1b) [2].

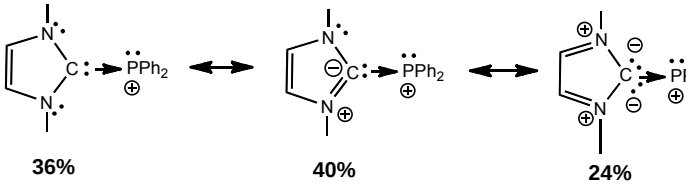

Figure 1a

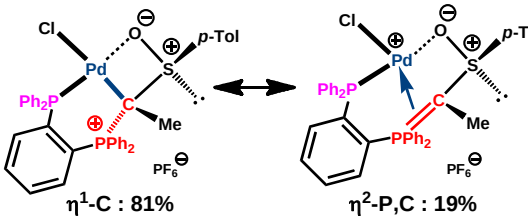

Figure 1b

Electronic properties may be discussed in terms of global metal-ligand electron transfer using infrared CO stretching frequencies in isostructural dicarbonylrhodium complexes [3]. ELF analysis, combined to fragment orbital analysis, allows for the distinction between donation and back-donation contributions within the framework of the Dewar-Chatt-Duncanson model [4]. In agreement with recent literature, a sizeable π-accepting character is found for NHCs.

[1] I. Abdellah, C. Lepetit, Y. Canac, C. Duhayon, R. Chauvin *Chem. Eur. J.* **2010**, *16*, 13985.
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BIO meets NANO at the Interface

Jerzy Leszczynski

NSF Interdisciplinary Nanotoxicity CREST Center, Department of Chemistry and Biochemistry, Jackson State University, 1325 Lynch St, Jackson, MS 39217-0510, USA

The DNA has been studied by computational approaches for almost 40 years. Though during this period computational chemistry has matured there are still areas needed improvements. Additionally, the new challenges of the 21th Century involve computational predictions for nanomaterials and their interactions with the biomolecules.

This talk provides a brief description of the results of our earlier theoretical studies on the DNA bases and highlights the most significant achievements and challenges related to our recent studies on interactions of DNA fragments with nanomaterials. Among studied species are DNA bases, fullerenes, carbon nanotubes, metal and metal oxide clusters.

[1] Nano Meets Bio at the Interface, Leszczynski J., *Nature Nanotechnology,* **2010**, *5*, 633-634.
[2] Novel view on the mechanism of water-assisted proton transfer in the DNA bases: bulk water hydration. A. Furmanchuk, O. Isayev, L. Gorb, O. V. Shishkin, D. M. Hovorun, J. Leszczynski, *Pyhs. Chem. Chem. Phys*. 2011, *13*, 4311-4317.
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[4] Density Functional Theory Investigation of Interaction of Zigzag (7,0) Single-Walled Carbon Nanotube with Watson-Crick DNA Base Pairs, Shukla M.K., Dubey M., Zakar E., Namburu R., Leszczynski J., *Chem. Phys. Lett.* **2010**, 496, 128-132.
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[6] DFT Investigation of the Interaction of Gold Nanoclusters with Nucleic Acid Base Guanine and the Watson-Crick Guanine-Cytosine Base Pair, Shukla M.K., Dubey M., Zakar E., Leszczynski J., *J. Phys. Chem. C*, **2009**, 113, 3960-3966.

Simulation of defect transport in stacked π-systems

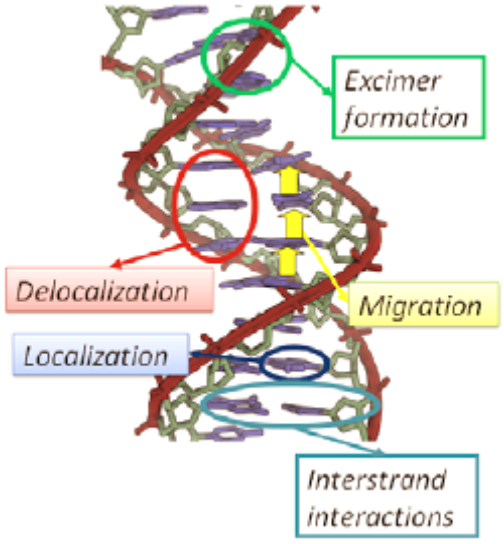
H. Lischka[a,b], A. A. J. Aquino[a,c], M. Ruckenbauer[b], F. Plasser[b]

[a]*Department of Chemistry and Biochemistry, Texas Tech University, 2500 Broadway, Lubbock, TX 79409, USA*

[b]*Institute for Theoretical Chemistry, University of Vienna, Waehringerstrasse 17, Vienna, A-1090, AUSTRIA*

[c]*Institute of Soil Research, University of Natural Resources and Life Sciences, Peter-Jordan-Strasse 82b, Vienna, A-1190, AUSTRIA*

The dynamics of defect migration in molecular systems has attracted widespread interest. For example, the transport of electron holes has been studied in DNA because of its relation to oxidative damage but also because DNA might provide interesting prototypes for nano-electronics. The defect structures induced by UV irradiation of DNA shown in the figure below play a crucial role in explaining the ultrafast pump-probe experiments.



The goal of the present investigations is to provide a picture of various defects as complete as possible based on extended *ab initio* calculations. The main features covered in the present contribution are (i) calculation of the electronic absorption spectra of stacked nucleobases in a DNA environment and analysis in terms of local, excitonic and charge-transfer excitations, (ii) stabilization of the charge-transfer (excimer) states by geometric relaxation and (iii) charge migration including nonadiabatic surface-hopping dynamics in model stacked ethylene systems.

The nonadiabatic dynamics simulations have been performed using the COLUMBUS [1] and NEWTON-X [2] program packages, the spectral calculations using TURBOMOLE [3]. In all cases a newly developed quantum mechanical/molecular mechanics (QM/MM) scheme with electrostatic embedding [4] has been used.

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[2] http://www.univie.ac.at/newtonx/
[3] http://www.turbomole.com/
[4] M. Ruckenbauer, M. Barbatti, Th. Müller and H. Lischka, J. Phys. Chem. A 114 (2010) 6757

Molecular energy decompositions

István Mayer

Chemical Research Center, Hungarian Academy of Sciences, H-1525 Budapest, P.O. Box 17, Hungary; e-mail: mayer@chemres.hu

The understanding and interpretation of the results obtained in a quantum chemical calculation can be much facilitated by presenting the total energy as a sum of chemically meaningful components. In the era of semiempirical quantum chemistry, this aim could be achieved trivially, as the semiempirical model Hamiltonians contained only one- and two-center integrals, so the different terms could be allocated to the atoms or pairs of atoms involved in a quite trivial manner. In *ab initio* theory, however, there are three- and four-center integrals, too, and in the straightforward energy component analysis of Clementi they led to the appearance of significant three- and four-atomic energy contributions, in sharp contradiction with the chemist's way of thinking of molecule as consisting of atoms exhibiting pairwise interactions.

The solution of this problem is difficult because we are lacking a unique definition of an atom within a molecule: one can perform the analysis either in the Hilbert space of the atomic basis orbitals or in the physical 3-dimensional (3D) space.

In the lecture I am going to summarize some of our results obtained in the last decade. First I will show the conceptually very important 3D result, according to which in the framework of Bader's "topological" AIM analysis, the SCF energy spontaneously decomposes into sum of atomic and diatomic contributions. In the Hilbert-space case the emphasis will be on the approximate CECA ("chemical energy component analysis") scheme, in which the the three- and four-center effects are compressed into one- and two-center ones as much as it is possible by performing appropriate projections. The further developments leading to an exact version of CECA and some other schemes will be briefly discussed, and a new, as yet unpublished, energy decomposition method will be presented essentialy for the first time, which contains some conceptually new elements permitting to overcome the difficulties connected with the previous schemes.

Modelling zwitterions in solution: 3-fluoro-γ-aminobutyric acid (3F-GABA)

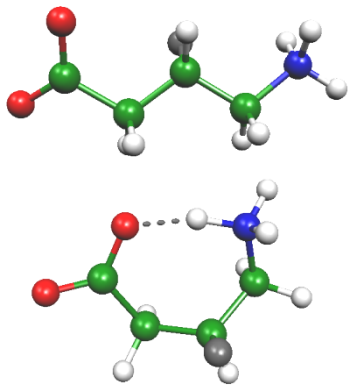
Tanja van Mourik[a], Jie Cao,[a] Ragnar Bjornsson, Michael Bühl[a], Walter Thiel[b]

[a]EaStCHEM School of Chemistry, University of St Andrews, North Haugh, St. Andrews, Fife, KY16 9ST, Scotland, UK

[b]Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470, Mülheim an der Ruhr, Germany

As the chief inhibitory amino acid in the mammalian central nervous system γ-aminobutyric acid (GABA) plays an important role in maintaining normal neuronal activity by controlling neuronal excitability. Information on how GABA binds to its receptors is very important for the design of novel agonists and antagonists, as well as for the development of neuropharmaceutical agents. Such information can be deduced from the binding of GABA analogues, such as 3-fluoro-γ-aminobutyric acid (3F-GABA), to the GABA receptors. In a recent study [1], the polarizable continuum model (PCM) was used at the B3LYP/6-31+G(d) level to study the different conformations of 3F-GABA in solution. It was found that the four most stable conformers found computationally are folded and contain an intramolecular hydrogen bond. However, comparison of computed and experimental NMR spin-spin coupling constants suggested that the dominant structure in solution is an extended conformer. This suggests that PCM may not give the correct order of stability of the different 3F-GABA conformers.

In this presentation, I will present results from calculations using explicit water molecules. Geometry optimisations were carried out at the M06-2X/6-31+G(d) level in the gas phase including up to five water molecules. Full explicit solvation was studied with a hybrid quantum-mechanical/molecular-mechanical (QM/MM) scheme and molecular dynamics simulations, including more than 6000 TIP3P water molecules. According to free energies obtained from thermodynamic integration at the PM3/MM level and corrected for B3LYP/MM total energies, the fully extended conformer is more stable than folded ones by ca. -9 kJ/mol. B3LYP-computed ^{3}J(F,H) NMR spin-spin coupling constants, averaged over PM3/MM-MD trajectories, agree best with experiment for this fully extended form, in accordance with the original NMR analysis. The seeming discrepancy between static PCM calculations and experiment noted previously is thus resolved.



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Consensus QSAR Modeling of Ames Mutagenicity

E.N. Muratov, D. Fourches, A.G. Artemenko, V.E. Kuz'min, G. Zhao, A. Golbraikh, P.G. Polischuk, E.V. Varlamova, I.I. Baskin, V.A. Palyulin, N.S. Zefirov, L. Jiazhong, P. Gramatica, T. Martin, F. Hormozdiari, P. Dao, C. Sahinalp, A. Cherkasov, T. Oberg, R. Todeschini, V. Poroikov, A. Zaharov, A. Lagunin, D. Filimonov, A. Varnek, D. Horvath, G. Marcou, C. Muller, L. Xi, H. Liu, X. Yao, K. Hansen, T. Schroeter, K.-R. Muller, I. Tetko, I. Sushko, S. Novotarskyi, J. Reed, J. Barnes, A. Tropsha

Affiliations are not shown because of limited abstract size; please, contact Alexander Tropsha for details: alex_tropsha@unc.edu

We report the results of a collaborative QSAR modeling project involving 15 research teams. Our goal was to develop predictive computational QSAR models of *in vitro* Ames mutagenicity induced by organic compounds. The Ames dataset, provided by Dr. K. Hansen from Technical University of Berlin, initially consisted of 7090 compounds classified as mutagenic or non-mutagenic. However, due to the presence of duplicates and incorrect structures, only 6542 compounds remained after curation of the original dataset using ChemAxon, HiT QSAR and ISIDA software. In total, 32 predictive classification QSAR models were developed using different combinations of chemical descriptors and machine learning approaches, representing the most extensive combinatorial QSAR modeling study ever done in the cheminformatics field in public domain. Although the resulting consensus model was not the best in training set fitting, it was the most externally predictive. Accuracy, sensitivity, and specificity were higher than 82% for both 5-fold external cross-validation and an external test set (100% coverage in both cases). These results confirmed our previous conclusions about the superiority of consensus modeling approaches in terms of prediction reliability. Model concordance analysis confirmed the stability of our Ames mutagenicity model. The second part of our study concerned the analysis of outliers defined here as compounds for which predictions by all models were in disagreement with their experimental annotation. Using both manual and automatic literature mining tools, we found published evidence indicating that 31 of 130 outliers (29 mutagens and 2 non-mutagens) were erroneously annotated in the original dataset. Our study provides a rare example of investigation, where developed QSAR models were successfully used for the correction of mis-annotated compounds in chemical databases. This work presents a model of collaboration that integrates the expertise of participating laboratories to establish the best practices and most reliable solutions for difficult problems in chemical and computational toxicology.

Theoretical chemistry of zeolite reactivity: from molecular understanding towards rational design

Evgeny A. Pidko

Inorganic Materials Chemistry, Eindhoven University of Technology P.O. Box 513, NL-5600 MB Eindhoven, The Netherlands, E-mail: e.a.pidko@tue.nl

The chemical reactivity of zeolite-based catalysts can be controlled by the introduction of extraframework metal-containing species into the microporous matrix [1]. For example, the introduction of Zn or Ga cations into high-silica zeolites induces their dehydrogenation activity. Zeolite modification with reducible iron species leads to uniquely selective oxidation catalysts, which are able to convert benzene to phenol and methane to methanol with high efficiency. Further improvement of these catalysts and the rational design of novel ones necessitate a deep insight into the role of the extraframework metal species in catalytic reactions. This, in turn, requires a clear picture of the molecular structure of these intrazeolite species as well as an understanding of the fundamental factors that control their structural and physicochemical properties. This however remains a challenge in the zeolite chemistry, especially in the case of high-silica zeolites.

By using state-of-the-art computational methodologies a deep molecular-level insight into the nature of catalytic sites, mechanisms of catalytic reactions can be obtained. In this lecture, the mechanisms of alkane dehydrogenation over gallium [2] and zinc-modified [3] high-silica zeolites and selective oxidation of benzene over zeolites modified with iron [4] will be discussed. With these relevant examples we will illustrate how thorough computational studies of the mechanism of catalytic reactions can lead to substantial improvements of real catalytic processes.

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Computer-aided approaches to virtual screening and rational design of multitargeted drugs

Vladimir Poroikov, Alexey Lagunin, Alexey Zakharov, Olga Koborova, Tatyana Gloriozova, Dmitry Filimonov

Institute of Biomedical Chemistry of Rus. Acad. Med. Sci., Moscow, Russia; e-mail: vladimir.poroikov@ibmc.msk.ru

Many diseases have a complex etiology, which treatment often requires multiple actions on several pharmacological targets. On the contrary, the majority of current drugs were designed to interact with a single target, which sometimes leads to activation/blockade of other elements in the appropriate signal regulatory pathway. As a consequence of negative feedbacks, expected pharmacotherapeutic effect may be significantly decreased or even completely suppressed. Therefore, the multitargeted drugs, due to their additive, synergistic or antagonistic action, might have some advantages comparing to the monotargeted medicines. The purpose of our study was to develop computer-assisted methods for identification of the most promising targets; finding and rational design of multitargeted agents with the required biological activity profiles.

The following computer-aided tools were used in this work. **Net2Drug** – software for simulation of behavior of signal regulatory pathways and identification of the most promising targets and their combinations. **PASS** (Prediction of Activity Spectra for Substances, http://pharmaexpert.ru/passonline/) - software, which predicts about 4000 kinds of biological activity on the basis of structural formula with mean accuracy about 95%. **PharmaExpert** – software for analysis of **PASS** predicted biological activity spectra and selection of compounds with the required biological activity profiles.

As a result, we identified the promising targets for treatment of breast cancers by analysis of signal regulatory pathways. Based on computer prediction of biological activity for 24 mln chemical compounds 64 molecules were selected for experimental testing. 26 samples were purchased and antineoplastic activity was confirmed experimentally in some molecules. Therefore, it was shown that computer-aided methods are rather useful in discovery of the most prospective pharmacological targets and their ligands.

Acknowledgements. This work was partially supported by European Commission FP6 grant LSHB-CT-2007-037590 (Net2Drug), FP7 grant 200787 (OpenTox), ISTC grants 3197 and 3777, RFBR grants 05-07-90123 and 06-03-08077.

Towards the development of Nano-QSAR models

T. Puzyn[a], D. Leszczynska[b] and J. Leszczynski[b]

[a] *Laboratory of Environmental Chemometrics, Faculty of Chemistry, University of Gdańsk, ul. Sobieskiego 18/19, 80-952 Gdańsk, Poland*

[b] *Interdisciplinary Center for Nanotoxicity, Department of Chemistry, Jackson State University, 1325 Lynch St , Jackson, MS 39217-0510, USA*

Nowadays, just 50 years after the Feynman's *"There's plenty of room at the bottom"*, nanotechnology has emerged at the forefront of science and technology developments and nanomaterials have found a wide range of applications in different aspects of human life. However, there is an increasing number of contributions that report toxicity and/or ecotoxicity of selected nanoparticles and highlight the potential risk related to the development of nanoengineering.

Quantitative structure-activity relationship (QSAR) methods can play an important role in both designing new products and predicting their risk to human health and the environment. But, regarding the specific properties of nanomaterials and their still unexplored modes of toxic action, this class of compounds seems to be much more problematic for QSAR modelers than the 'classic' (relatively small, drug-like) chemicals.

This presentation discusses current advances and challenges of QSAR development for nanomaterials (Nano-QSAR). The most challenging problems are: (i) scarce and/or inconsistent experimental data available and lack of conceptual frameworks for grouping nanoparticles according to mode of physicochemical properties and toxic action; (ii) lack of appropriate descriptors able to express specificity of "nano" structure; (iii) very limited knowledge on the interactions between nanoparticles and biological systems (DNA, proteins, membranes etc.); and (iv) lack of rational modeling procedures to screen large numbers of structurally diversified nanoparticles. Majority of the existing Nano-QSARs refer to physical-chemical enpoints. However, our last contribution demonstrated the first Nano-QSAR model for predicting toxicity (cytotoxicity to bacteria E. coli) of nano-sized metal oxides. This would be the first step towards creating a comprehensive tool for computational risk assessment of nanomaterials to be used for regulatory purposes.

Computational chemistry as a tool for designing functionalized materials

Szczepan Roszak, Paweł Kadłubański, Rafał Roszak and Andrzej Drabarek

Institute of Physical and Theoretical Chemistry, Wrocław University of Technology, Wyb. Wyspiańskiego 27, 50-370 Wrocław, Poland; e-mail: szczepan.roszak@pwr.wroc.pl

The carbon nanomaterials exhibit promising properties for potential applications in modern technologies. These properties are additionally enhanced by the foreign atoms doping. The evolution of bonding and thermodynamic properties of C_nB, B_nC, and B_nSi was studied with the aim to elucidate possible roads of the clusters grows. The B, N, Be, and H doping of carbon nanotubes and graphene fragments was investigated and its influence on electronic properties, reactivity, and hydrogen adsorption properties was determined. The local and global properties of modified carbon materials were investigated. Additionally, possible mechanisms and thermodynamics of hydrogen oxidation and oxygen reduction on graphene surfaces were examined. The presented studies were performed as part of search for practical materials, useful for hydrogen storage and fuel cells construction.

Thermodynamic and evolutionary aspects of structure fluctuations in proteins

Anatoly M. Ruvinsky[a] and Ilya A. Vakser[a,b]

[a]Center for Bioinformatics and [b]Department of Molecular Biosciences, University of Kansas, Lawrence, KS; e-mail: ruvinsky@ku.edu

Structure fluctuations in proteins affect a broad range of cell phenomena, including stability of proteins and their fragments, allosteric transitions, and energy transfer. This study addresses thermodynamic and evolutionary aspects of relation between protein sequence, structure fluctuations and instabilities in proteins and their complexes.[1] Structure fluctuations are characterized by a novel elastic network model accounting for the protein mass distribution and the interatomic interactions by utilizing renormalized inter-residue Tirion-like potential. The results indicate that the residue mass and its structural environment determine the scale of the residue fluctuations. Surface residues undergo larger fluctuations than the core residues in agreement with experimental observations.

A new fluctuations-based classification of amino acids was established. It includes three groups of residues: (i) highly fluctuating - Gly, Ala, Ser, Pro, and Asp, (ii) moderately fluctuating - Thr, Asn, Gln, Lys, Glu, Arg, Val, and Cys, and (iii) weakly fluctuating - Ile, Leu, Met, Phe, Tyr, Trp, and His. The biased distribution of these groups in proteins allows us to hypothesize that (a) the structural instabilities in proteins relate to high content of the highly fluctuating residues and a lack of the weakly fluctuating residues in protein loops, chameleon sequences and disordered proteins, and (b) the nucleation of the unfolded phase originates from protein loops and clusters of the highly fluctuating residues. The results point to strong correlation between the residue fluctuations and the sequence composition of protein loops. This supports the hypothesis on the origins of unfolding, and explains the inability of such sequences to form ordered secondary structure elements (α-helices or β-strands).

Fluctuations of binding site residues were shown to be, on average, smaller than the fluctuations of the non-interface surface residues. The increased interface rigidity largely relates to Gly, Ala, Ser, Cys, Leu, and Trp, and leads to formation of stable docking patches to facilitate binding. The findings provide a better understanding of protein structures thermostability and binding mechanisms.

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Supramolecular architecture of molecular crystals derived from analysis of intermolecular interactions energy

Oleg V. Shishkin

Division of Functional Materials Chemistry, SSI "Institute for Single Crystals," National Academy of Sciences of Ukraine, 60 Lenina ave., Kharkiv 61001, Ukraine; e-mail:shishkin@xray.isc.kharkov.com

Common approach to description of crystal structure of molecular crystals is based on analysis of distances between atoms of neighbouring molecules in order to determine possible intermolecular interactions like hydrogen or halogen bonds, stacking interactions etc. Taking into account high accuracy of modern X-ray diffraction studies this method allows in most cases to find the strongest intermolecular interactions describing of crystal structure as packing of strongly bonded molecules. However, in the case of absence of such more or less strong interactions such geometrical approach is almost completely useless and structure of crystal may be described in some arbitrary way depending on aesthetic view of specific investigator.

Recently [1-3] it was suggested much more rigorous way for analysis of supramolecular architecture of molecular crystals based on accurate calculations of intermolecular interaction energies between basic molecule located in asymmetric part of unit cell and all molecules belonging to its first coordination sphere. Determination of molecular environment in crystal is based ob calculations of Dirichlet polyhedron of basic molecule. Energy of interactions is calculated using DFT or MP2 methods allowing correct description of dispersion interactions.

Application of this method to crystals of hydrocarbons and their heterocyclic analogues provides clear recognition of main packing pattern namely layers and columns where energy of intermolecular interactions of basic molecule with neighbours within this fragment is considerably higher than to molecules belonging to other such fragments. This allows describing supramolecular architecture of molecular crystals in unambiguous way as packing of strongly bonded layers or columns even in the case of existence of hydrogen bonded dimers, for example, in crystals of polymorphic modifications of the 3,4-diamino-1,2,4-triazole.

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Importance of electrostatic effects in modeling molecular materials

W. Andrzej Sokalski

Wrocław University of Technology, Wyb. Wyspianskiego 27, 50-370 Wroclaw, Poland

Various properties of matter, like recognition of biomolecules, structure and cohesion energy of molecular crystals, activity of biocatalysts, drugs are determined by intermolecular forces. Due to large size of interacting systems involved corresponding computational studies are very costly and most frequently limited to approximate methods of empirical character which are not capable to represent all physical effects correctly. Therefore proper understanding of existing limitations requires detailed analysis of all interaction energy components. The knowledge of the physical nature of interactions involved may open the possibility to derive in systematic way new approximate models aiding rational design of new materials.

On the use of electronic delocalization indices of aromaticity in all-metal clusters

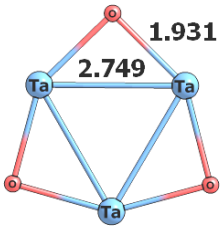
M. Solà[a], F. Feixas[b], E. Matito[b], J. Poater[a]

[a] *Institut de Química Computacional and Departament de Química, Universitat de Girona, Campus de Montilivi, Girona, 17071, Catalonia, Spain*

[b] *Kimika Fakultatea, Euskal Herriko Unibertsitatea, P.K. 1072, 20018 Donostia, Euskadi, Spain*

Aromaticity is a central concept in a central science such as Chemistry. Aromaticity is widely used in modern chemistry for the interpretation of molecular structure, stability, reactivity, and magnetic properties of many compounds. As such its reliable prediction is an important task of theoretical chemistry. In recent years, many methods to quantify aromaticity based on different physicochemical properties of molecules have been proposed. However, the non-observable nature of aromaticity makes difficult to assess the performance of the numerous existing indices to measure it.[1] This is especially true in the case of the recently discovered all-metal and semimetal aromatic clusters for which the presence of multifold aromaticity and the lack of reference systems (like benzene in classical aromatic organic molecules) make the measure of aromaticity much more complicated.

In this presentation we first analyze the advantages and drawbacks of electronic and other aromaticity descriptors to measure the aromaticity of classical organic molecules and all-metal clusters. Our results show that, in general, indices based on the study of electron delocalization are the most accurate to describe aromaticity in classical organic molecules and inorganic clusters.[2,3] Moreover, it is found that these indices are excellent indicators of σ-, π-, and δ-type of aromaticity in all-metal clusters.[4]



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Quantum-chemical calculations on nucleic acids sugar-phosphate backbone. From reference computations to refinement of the molecular mechanics force fields

Jiří Šponer

Institute of Biophysics, Academy of Sciences of the Czech Republic, Královopolská 135, 61265 Brno, Czech Republic; e-mail: sponer@ncbr.chemi.muni.cz

Properties of nucleic acids are significantly affected by their sugar-phosphate backbone. Studies of backbone conformations are, however, still relatively rare and difficult. From the structural biology and bioinformatics point of view, backbone is a difficult target due its inherent flexibility and associated data and refinement errors in structure determination. While bases and phosphorus atoms are usually well visible in electron densities, the other backbone atoms are not. The polarizable anionic and flexible backbone chain is also difficult to describe by non-polarizable force fields utilizing atom-centered constant point charges. Nucleic acid backbone is also very difficult for QM calculations, due to its flexibility and complexity of the potential energy surfaces, its anionic nature, propensity to form spurious intramolecular H-bonds with no biochemical relevance and intramolecular basis set superposition error.

I will review our current reference QM calculations on nucleic acid backbone and major refinements of the Cornell et al AMBER force field for nucleic acids, known as parbmsc0 and parmOL, which are critically important to stabilize nucleic acids simulations. Parmbsc0 refines the α/γ torsional space and prevents DNA degradation while parmOL refines the χ dihedral torsion and prevents degradation of RNAs in simulations.

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Interaction between molecular oxygen and the (111) and (100) faces of crystalline silicon

Terebinska M.I., Tsendra O.M., Lobanov V.V.

Chuiko Institute of Surface Chemistry, National Academy of Sciences of Ukraine, 17 General Naumov Str. Kyiv, 03164, Ukraine

Among the interactions of molecular oxygen and silicon, the surface reactions between molecular oxygen and the (111) and (100) faces are perhaps the most common. A theoretical study was undertaken in this work in order to elucidate the nature of this interaction.

The energies of formation of the molecular complexes [111·O_2] and [100·O_2] and their subsequent reaction products were calculated with the density functional theory (DFT) using the B3LYP approach and the 6-31 G** basis sets. These molecular complexes are formed on the first stages of interaction between molecular oxygen and the (111) and (100) faces of crystalline silicon. It was found that the O_2 molecule is located parallel to the surface plane on both faces of crystalline silicon. A significant transfer of electron density from the crystal to the O_2 molecule is observed, that leads to the elongation of the O–O bond of the chemisorbed molecule as compared to free O_2.

In a second step the O_2 molecule is dissociated into atoms, each one being associated to silicon surface atoms. The formation of a top-top structure on the (111) face has a potential barrier of ~0.2 eV, while on the (100) face this process has no barrier. Ins-ins structures are then formed and oxygen atoms intrude into the Si–Si bonds adjacent to the Si-atom. Then a second O_2 molecule is adsorbed in the vicinity of the formed Si–O bonds. The energy changes of these reactions are 4.1 and 4.2 eV for the partly oxidized (111) and (100) faces, respectively. The subsequent transformations of surface supramolecular structures with the second O_2 molecule are analogous to the initial process of oxidation of silicon. The analysis of the equilibrium structure of the cluster models of the adsorption complexes [111·O_2] and [100·O_2] and their subsequent reaction products indicates that the oxidation of the (111) and (100) silicon faces by molecular oxygen is spontaneous and that the process of formation of the oxide phase is rather an insular one.

Calculation of the IR-spectrum of surface structures of oxygen on the (111) and (100) silicon faces by means of the harmonic approximation showed the existence of strong interaction between the oxygen top-atoms and the crystal lattice. The calculated frequencies of the adsorbed oxygen structures were found to be considerably different than the vibration frequencies of interstitial oxygen atoms. This difference is especially noticeable for top-top and top-ins structures that have ≡Si–O bonds located perpendicular to the surface.

A study of the interaction of the O_2 molecule with the surface of crystal silicon within the DFT framework was performed using the Born-Oppenheimer approximation. According to this approximation the changes in configuration of the nuclei of the O_2 molecule vary according to the profile of a Potential Energy Surface (PES) for the ground electronic state (GES). The GES for the O_2 molecule is a triplet and for the molecular complexes [111·O_2] and [100·O_2], a singlet.

The order of the three lowest levels ${}^3\sum_g^-$, ${}^1\Delta_g$ and ${}^1\sum_g^+$ of the O_2 molecule changes dramatically when approaching the surface. The calculations show that an intersection of the PESs occurs. This means that the energy change of the cluster "(111)+O_2" firstly goes along an diabatic curve of the excited triplet state and only at a certain distance between the O_2 molecule and the surface the system goes on a lower adiabatic curve of the ground singlet state.

Adsorption of amino acids on the TiO_2(110) surface

Ralf Tonner

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein Straße, 35032 Marburg, Germany; E-mail: tonner@chemie.uni-marburg.de

Titanium dioxide is the most investigated single-crystalline metal oxide in surface science - experimentally as well as theoretically. For the low index surface (110) a reliable structural model exists [1]. The optimal adsorption modes for amino acids glycine and proline on the ideal TiO_2(110) surface have been investigated using density functional theory (PBE) applying periodic boundary conditions (VASP) [2]. Binding modes with anionic acid moieties bridging two titanium atoms after transferring a proton to the surface are the most stable configurations for both molecules investigated similar to previous results for carboxylic acids.

In contrast to the latter, amino acids can form hydrogen bonds via the amino group towards the surface-bound proton which provide an additional stabilization of 15-20 kJ mol^{-1}. Zwitterionic binding modes are less stable by 10-20 kJ mol^{-1} and are less important for proline. Neutral modes are energetically even less favorable. Calculations of vibrational frequencies complement the adsorption study and provide guidance for future experimental investigations. Control of the computational parameters is crucial for the derivation of accurate results and the layout and thickness of the slab model used is shown to be the decisive factor here. Calculations with PW91 provide very similar relative energies while PBE0 results prefer the anionic modes even stronger.

A previously observed discrepancy between experimental and theoretical results for glycine could be solved, although the experimentally proposed free rotation of the C-C bond could not be reproduced. In a broader context, the present study can be regarded as a primary model for the interaction of peptides with titanium-based implants which exhibit an oxide layer [3].

An investigation of the adsorption processes on a molecular level even in idealized conditions can help in understanding these complex reactions.

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On categorization of chiral and achiral substituted derivatives of rigid organic skeletons

Serge S. Tratch, Nikolai S. Zefirov

Department of Chemistry , M.V. Lomonosov Moscow State University, 1 Leninskie Gory, Moscow 119992, Russia

It was V. Prelog (Nobel Prize Lecture, 1975) who for the first time demonstrated [1] the existence of three categories of chiral and two categories of achiral substituted methanes with achiral as well as chiral substituents. Using more advanced approach, with new notions of *sclerality* and *RS-stereogenicity* being introduced, S. Fujita has later shown [2] that only three and two types of *stereoisograms* can be assigned to chiral and achiral derivatives of methane and many other organic skeletons (ethylene and allene derivatives may serve as examples). It can be shown, however, that S. Fujita's original definition of RS-steregenicity prevents his approach to be applied to more complicated cases, especially those associated with bi- and polycyclic skeletons (norbornadiene and prismane derivatives may serve as examples).

In the present lecture, we explicitly demonstrate that just three and two categories are respectively possible for chiral and achiral derivatives of ANY rigid skeleton. The rigorous proof is based on five subgroups of the *Generalized Transformation Group* of order 4; the elements of the latter group either leave the initial skeleton or / and the set of all substituents unchanged or convert it (or them) into corresponding mirror image(s). For illustration purposes, many examples of actual chiral / achiral, scleral / ascleral, and *twinal / atwinal* substitution products (the latter ones correspond to S. Fujita's RS-stereogenic / astereogenic derivatives) are also displayed.

The simple algorithms making it possible to recognize categories for particular derivatives of any given achiral 2D or 3D and also of chiral 3D skeletons are considered in the lecture. The specific kinds of stereoisomerism corresponding to chiral antipode derivatives (i.e., enantiomers), scleral antipode derivatives (S. Fujita's *holantimers*), and twinal antipode derivatives (referred to as *nullantimers*) are additionaly discussed. Finally, it is shown that not only well-known enantiomerization and racemization processes but also similar interonversions of hoantimers and nullantimers should be experimentally realizable; the suggested models are based on inversion of the 6-membered cycle in cis-1,2- and trans-1,3-disubstituted cyclohexanes with two identical or enantiomeric chiral substituents.

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Reconstruction of the Pauli and Quantum Potentials from Experimental Electron Density

Vladimir G. Tsirelson[a], Adam I. Stash[a,b]

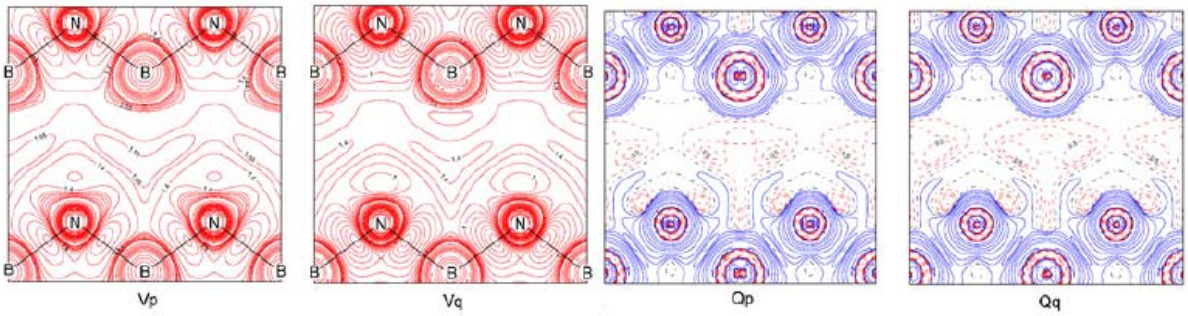
[a] *D.I. Mendeleev University of Chemical Technology, Moscow, Russia*

[b] *L. Ya. Karpov Institute of Physical Chemistry, Moscow, Russia*

In DFT, the total energy can be presented as a sum of the independent energy contributions $E[\rho]=E_{el}[\rho]+E_s[\rho]+E_q[\rho]$, each of them is a functional of electron density, $\rho(\mathbf{r})$. $E_{el}[\rho]$ describes the classic electrostatic electron-electron, nuclear-electron and nuclear-nuclear interaction energies. The term $E_s[\rho]$ measures the intrinsic dimensions peculiar to the system, when the quantum and electrostatic effects are completely excluded and can be attributed to the "kinetic energy pressure" experienced by a confined atom/molecule from the surrounding. $E_s[\rho]$ is associated with the steric effect and is described by the Weizsäcker kinetic energy $E_s[\rho]=T_W[\rho]=\frac{1}{8}\int\frac{|\nabla\rho(\mathbf{r})|^2}{\rho(\mathbf{r})}d\mathbf{r}$. Quantum energy contribution, $E_q[\rho]=E_{xc}[\rho]+E_P[\rho]$, is the sum of the exchange-correlation energy $E_{xc}[\rho]$, including a kinetic counterpart of the dynamic electron correlation, and the Pauli energy, $E_P[\rho]=T_S[\rho]-T_W[\rho]$, which is the contribution to the kinetic energy from the Pauli Exclusion Principle ($T_S[\rho]$ is non-interacting kinetic energy of electrons).

The Pauli potential can be defined as the functional derivative of the Pauli energy with respect to the electron density: $v_P(\rho,\mathbf{r})=\frac{\delta E_P(\rho,\mathbf{r})}{\delta\rho}=\frac{\delta T_S(\rho,\mathbf{r})}{\delta\rho}-\frac{\delta T_W(\rho,\mathbf{r})}{\delta\rho}$, where $\frac{\delta T_W(\rho,\mathbf{r})}{\delta\rho}=\frac{1}{8}\frac{|\nabla\rho(\mathbf{r})|^2}{\rho^2(\mathbf{r})}-\frac{1}{4}\frac{\nabla^2\rho(\mathbf{r})}{\rho(\mathbf{r})}$ is the steric potential. By analogy, the quantum potential (putting the chemical potential μ=0) is $v_q(\rho,\mathbf{r})=\frac{\delta E_q(\rho,\mathbf{r})}{\delta\rho}=\frac{\delta E_{xc}(\rho,\mathbf{r})}{\delta\rho}+\frac{\delta E_P(\rho,\mathbf{r})}{\delta\rho}$.

In this work, we explore the opportunity to derive the Pauli and quantum potentials from experimental electron density. We consider the two methods. The first one consists of approximating the kinetic energy density by the gradient expansion. The second one is based on approximating the exchange correlation potentials with the known local DFT functionals: we have applied the (local) von Barth-Hedin exchange and correlation potentials. We have also computed the charge densities associated with these potentials. Application this approach to crystals with different types of chemical bonds will be discussed; corresponding pictures for BN are given below.



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First principle study of structure and interconversion of native cellulose phases

Tomáš Bučo,[a,b,c] Daniel Tunega,[b,d] Jürgen Hafner,[c] and János G. Àngyán[e]

[a]*Department of Physical and Theoretical Chemistry, Faculty of Natural Sciences, Comenius University, Mlynská dolina, SK-84215 Bratislava, Slovakia*

[b]*Institute of Inorganic Chemistry, Slovak Academy of Sciences, Dúbravska cesta 9, SK-84236 Bratislava, Slovakia*

[c]*Fakulty for Physics and Center for Computational Materials Science, University of Vienna, Sensengasse 8, A-1090 Vienna, Austria*

[d]*Institute for Soil Research, University of Natural Resources and Life Sciences, Peter-Jordan-Strasse 82, A-1190 Vienna, Austria*

[e]*Équipe de Modélisation Quantique et Cristallographique, CRM2, Institut Jean Barriol, UMR 7036, CNRS - Nancy-Université, B.P. 239, F-54506 Vandœuvre-lès-Nancy, France*

Cellulose is a natural biopolymer forming a substantial part of plants and trees. Owing to its low weight, specific mechanical properties, and fibrous structure it found numerous applications ranging from paper industry to medicine and biotechnology. Cellulose belongs to polysaccharides with D-glucopyranose units linked via glycosidic bond. So far four basic crystalline forms have been indentified [1]. The native cellulose exists in two allomorphic phases I_α and I_β and their relative ratio depends on the source of cellulose [1]. In cellulose three basic chemical interactions meet together – polar covalent bonds, hydrogen bonds, and weak van der Waals interactions.

In this work we report a DFT study of the structures of the I_α and I_β phases and of the corresponding phase transformation. From the computational point of view the most problematic is a correct description of van der Waals forces by standard DFT functionals. These forces play a crucial role in the stabilization of the three-dimensional lattice structure of cellulose. In order to fix this problem, a semi-empirical correction to van der Waals interactions (PBE-D2) proposed by Grimme [2] has been used in this work. The transition mechanism for the conversion between the I_α and I_β phases has been studied by means of constrained relaxations and *NpT* molecular dynamics.

A good agreement between theoretical (PBE-D2) and experimental structural data has been achieved and two H-bond patterns, previously identified experimentally, have been examined for both allomorphs. In the phase transformation, two mechanisms have been found. The first mechanism is identified as irreversible with an existence of an intermediate metastable phase while the second one is direct and quasi-reversible. The energy difference between the transition barriers of two mechanisms is comparable with the thermal energy $k_B T$, therefore, an accurate account for the thermal effects would be needed to decide which route is more likely in nature.

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Fragmentation of negative ions induced by electron capture – theoretical description

J. Urban[a], P. Mach[a], P. Papp[a], and J. Horáček[b]

[a]*Faculty of Mathematics, Physics and Informatics, Comenius University, Bratislava, Slovakia*

[b]*Faculty of Mathematics and Physics, Charles University, Prague, Czech republic*

Resonances play important roles in many physical and chemical processes. Some processes are very efficient (vibrational excitation of molecules by low energy electrons, dissociative electron attachment, the process of associative detachment, dissociative recombination). To describe the above mentioned-processes knowledge of resonance energies and resonance width of molecular anions is required. Generally, the calculation of these resonance parameters is a very complicated problem. This is because of the nature of the resonance wave function which is not, contrary to a bound state wave function, a square integrable function vanishing at infinity but in fact exponentially diverging at large distances. Several methods have been developed in the last four decades to calculate resonance energies. In the contribution we summarize the mostly used approaches for the study of negative ions in the process of dissociative electron attachment. In our contribution the simple schemes for the calculation of resonance energies and resonance widths are applied. First, consisted on the stabilization of the resonance orbital energy by the increased nuclear charge originally proposed by Nestmann and Peyerimhoff [1] and the second approach [2] where the attractive short-range potential U(r) multiplied by a real positive parameter λ is added to the original potential V(r) and at increasing λ some resonance states may transform into bound states. Idea of this analytic continuation in the coupling constant (ACCC) method was proposed in the field of nuclear physics by Krasnopolsky and Kukulin [3,4]. The advantage as well as the drawback of methods applied to the chosen molecules is discussed. Methods are applied also to the biomolecules where the effect of electron capture may cause the formation of negative and positive ions following the fragmentation of molecules.

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[3] V. M. Krasnopolsky, and V. I. Kukulin, Phys. Lett. **69A**, 251-254 (1978)
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Prediction of protein-ligand interaction fingerprints

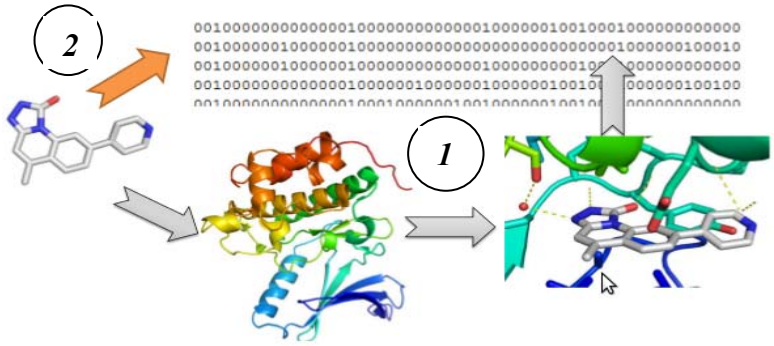
A. Varnek [a], V. Chupakhin [a,b], G. Marcou [a], I. Baskin [a], D. Rognan [b]

[a] *Laboratory of Chemoinformatics, UMR 7177 CNRS-UdS, Strasbourg*

[b] *Structural Chemogenomics Group, UMR 7200 CNRS-UdS, Illkirch*

Docking of compounds to the protein is an efficient method of structure-based virtual screening. Typically, it proceeds into two main steps: (a) finding the binding poses; and (b) assessing the binding efficiency using a scoring function. Practically all known scoring functions contain empirical parameters fitted on relatively small sets of experimental data and, therefore, they often fail to predict binding affinities for the ligands structurally different from the training set compounds. An alternative way to guide the docking and to estimate protein-ligand binding is based on the Interaction Fingerprints (IPFs) approach. An Interaction Fingerprint is a bitstring encoding 3-D information of some protein-ligand interactions (hydrophobic, aromatic, H-bond and electrostatic interactions). Any similarity measure (Tanimoto, Dice, etc) can be used to compare different fingerprints. Usually, IFP are generated from the X-ray or modeled structure of the protein-ligand complex.

Here, we describe the method of predicting IFP for the ligands solely using QSAR models built on a training set of several protein-ligand complexes. Application of this approach to the ligands for three protein targets (CDK2, MAPK14, HSP-90) is discussed.



Interaction Fingerprints generated (1) from the structure of protein - ligand complex, or (2) using QSAR models

[1] Ferrara, P. et al. *J Med Chem*, 2004, **47**:3032-3047.
[2] Marcou, G. and D. Rognan, *J. Chem. Inf. Model*, 2007. **47:**195-207.
[3] Varnek, A., et al., *Current Computer-Aided Drug Design*, 2008, **4** (3), 191-198.

Application of CCT Technique to Simulate Vibrational Spectra of Nucleic Acid Oligomers

V. Andrushchenko and P. Bouř

Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Flemingovo nam. 2, Prague, 16610, Czech Republic; e-mail: andrushchenko@uochb.cas.cz, bour@uochb.cas.cz

Vibrational spectroscopy plays an important role in investigation of the structure and conformational changes of nucleic acids due to rich structural information it provides, a wide availability, and relatively fast acquisition times. However, due to complexity of the nucleic acid vibrational spectra, large bandwidth, many overlapping vibrational bands and coupling of vibrations, clear and straightforward interpretation of the spectra with respect to the nucleic acid structure and dynamics is an ambiguous and tedious task. Theoretical simulations of the spectra can significantly simplify this task allowing for unambiguous assignment of spectral features to vibrations of particular DNA and RNA functional groups and additionally providing rich information on the system's energetics and interactions obtained from the first principles. However, such simulations are limited by a large size of the molecules, which becomes a main challenge when dealing with nucleic acids and other biological molecules. One of possible approaches to overcome this limitation, Cartesian coordinate transfer (CCT) technique has been developed in our group [1]. The method is based on transferring molecular properties from smaller molecular fragments to larger systems. This allows one to compute vibrational spectra for relatively long oligomers of nucleic acids, which would be inaccessible by direct ab initio simulations with required precision. The application of CCT method will be illustrated on several examples, including single-, double- and multiple-stranded conformations of both DNA and RNA systems. It will be also demonstrated how molecular dynamics (MD) simulations performed prior to ab initio calculations allow one to account for the system's dynamics and result in better agreement between the simulated and experimental spectra.

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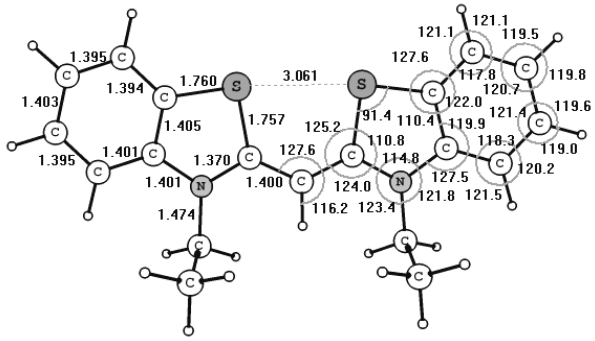
Structure and spectral bands shifts for dimers and aggregates of monomethyne and carbocyanine dyes

Vitaly G. Avakyan[a], Mikhail V. Alfimov[a], and Boris I. Shapiro[b]

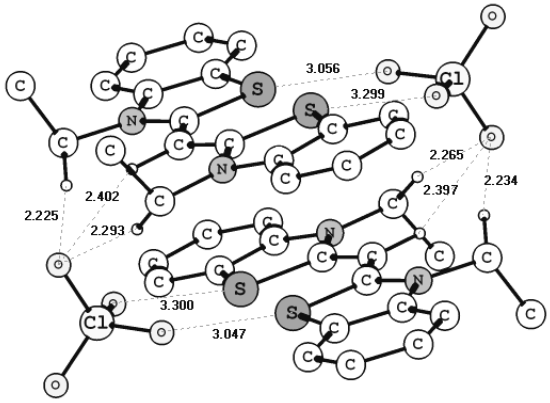
[a]Photochemistry Center of RAS, Moscow, Russian Federation. [a]avak@photonics.ru

[b]Scientific Center NIIKHIMPHOTOPROJECT, Moscow, Russian Federation

This study is carried out to predict a structure of free dimers and tetramers of series of carbocyanine dyes capable to form both dimers (H-aggregate) revealed by blue shift as compared to monomer band and J-aggregates identified by red shift of absorption band. Objects were benzothiacyanine (**I**), thiazolincarbocyanine (**II**), and benzothiazolincarbocyanine perchlorates. Methods of calculation were DFT with exchange-correlation functional PBE, semi-empirical methods PM3 with standard set of parameters (optimization of monomer, dimer and tetramer structures) and ZINDO/S (calculation of the transition energies of monomers and aggregates).



Monomer



ΔH_0 –18.4 kcal/mol (*DFT/PBE*)

Took as an example, stacking dimer **I** is formed in antiparallel configuration with slip angle ~14º between participants (symmetry C_i, distance between components ~4.1 Å). In the second dimer structure, slip angle is increased up to 30º. ZINDO/S calculation (CI active space 22x22 orbitals, 969 configurations) predicts that dimer absorption band is expected to be blue shifted by 12.5 nm as compared to monomer band (436.9 nm). An increase of slip angle between dimer participants to 32º results in an increase of the absorption wavelength to 444.6 nm. Since analyses of experimental data demonstrate that J-aggregates are built as brick work structure (BWS) formed from dimers, we performed a search (DFT & PM3) for tetramer structure. It was shown that the like BWS structural motif of packing **I** maintains stability only in the middle of decamer (see picture below). Its formation energy –93.1 kcal/mol (PM3). ZINDO/S calculation of BWS tetramer (CI active space 44x44 orbitals, 3873 configurations) predicts that tetramer absorption band is expected to be red shifted by 22.3 nm (459.2 nm) respectively to monomer band. For BWS of heptamer **II** (λ_{max} 485 nm), a red shift of absorption band was predicted to be 59 nm. This behavior resembles to the red shifts of J-aggregate absorption bands observed in water solution.

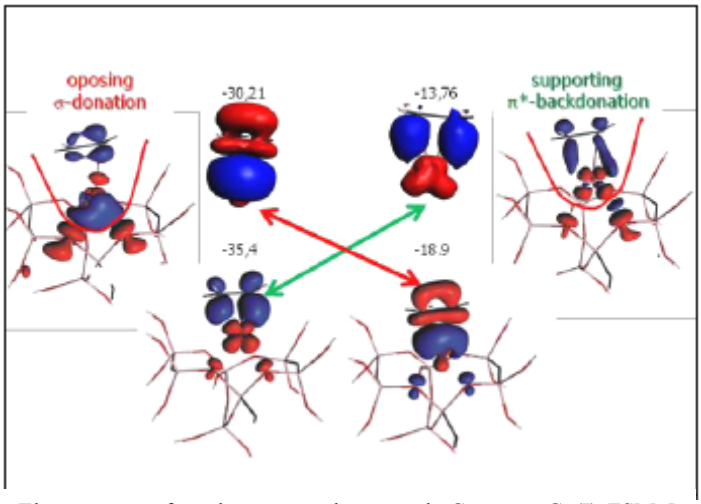
Charge Transfer in Substrate Binding and Activation by Cationic Sites in Zeolites: ETS-NOCV Perspective

E. Broclawik[a], J. Załucka[b], P. Kozyra[b], M. Mitoraj[b] and J. Datka[b]

[a] *Institute of Catalysis, Polish Academy of Sciences, Niezapominajek 8, 30-239 Krakow*

[b] *Faculty of Chemistry, Jagiellonian University, Ingardena 3, 30-060 Krakow, Poland*

Charge transfer between the active site and a substrate results from delicate balance in individual electron transfer processes. We apply new electron density analysis (ETS-NOCV) with flexible strategy of dividing multicomponent system (zeolitic active site) into fragments. It decomposes total electron transfer upon adsorbate bonding, into independent channels, showing various impact on substrate bonding and activation. Two alternative fragmentation schemes of three-component embedded cluster models of Cu(I) and Ag(I) sites in zeolites hosting ethene, ethyne or formaldehyde, provided insight into charge transfer between the substrate and a site or between framework oxygens and a cation [1-3]. In this contribution we present cross-analysis of charge transfers between the substrate, the cation and framework oxygens, with the focus on the influence of zeolite on donation/backdonation processes, tuning properties of embedded cation and thus the activity of Me(I) sites.



Electron transfers between ethene and Cu+ or Cu(I)-ZSM-5 (up/down); red and blue represent electron outflow/ inflow. Left and right insets illustrate the role of framework oxygens.

Insets in the figure beside illustrate two dominant electron transfer channels from framework oxygens to Cu(I) cation: opposing σ-donation of ethene bonding electrons and supporting π*-backdonation to antibonding ethane orbitals (shown in main window). While the latter enhances substrate activation (evidenced by IR red-shift), the former weakens activation ability of the cation upon embedding in zeolite framework. Thus the activity of a cationic site must be viewed as resulting from framework effect on the sensitive balance between opposing electron transfer channel Detailed cross-analysis for the three substrates showed that activation decrease due to reduction of σ-donation was outweighed by the increase in π*- backdonation for Cu(I) but not for Ag(I).

Our results indicate clearly that zeolitic framework regarded as an electron reservoir may either support (Cu+) or impair (Ag+) electronic processes underlying catalysis. Therefore enhancing effective activity of zeolitic cationic sites requires designed tuning of as well its σ-donation as π*- backdonation ability by smart manipulation with the framework properties.

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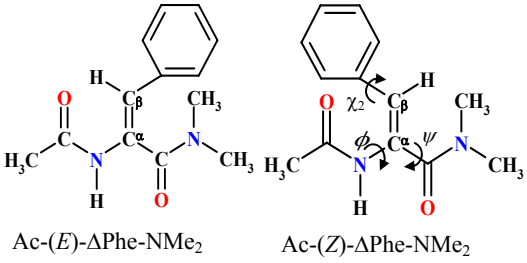
Experimental and theoretical studies on the conformational properties of the *E* and *Z* isomers of dehydrophenylalanine residue

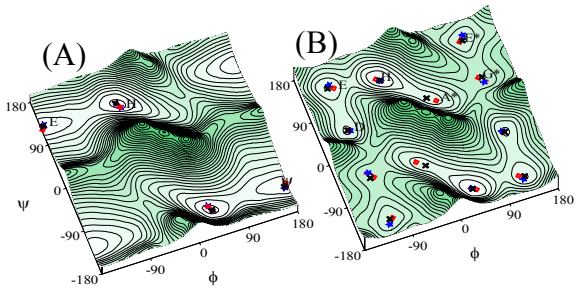
Aneta M. Buczek[a], Tomasz Ptak[a,b], Teobald Kupka[a], Małgorzata A. Broda[a*]

[a] *Faculty of Chemistry, University of Opole, Oleska 48, 45-052 Opole, Poland*

[b] *Department of Basic Medical Sciences, Medical Academy, Kochanowskiego 14, 51-601 Wroclaw, Poland*

Conformation of *N*-acetyl-(*E*)-dehydrophenylalanine *N',N'*-dimethylamide (Ac-(*E*)-ΔPhe-NMe_2) in solution, a member of (*E*)-α,β-dehydroamino acids, was studied by NMR and IR spectroscopy and the results were compared with those obtained for (Z) isomer.





The general formula and selected torsion angles of the studied molecules are given in Figure 1. The E=*f*(ϕ,ψ) potential energy surfaces (PES) of the studied (*E*) and (*Z*) isomers of Ac-ΔPhe-NMe_2 calculated in chloroform environment are shown in Fig. 2A and B, respectively. The conformational maps of *E* and *Z* isomers reveal two and six minima (and theirs mirror counterparts), respectively. For both isomers the most preferred conformation is calculated to be H (ϕ, ψ ≅ –40º, 130º). This conformation is stabilized mainly by dipole interaction between carbonyl groups, and additionally, by the NH···π H-bond in the case of Z isomer.

The IR spectra of Ac-(*E*)-ΔPhe-NMe_2 in CCl_4 and $CHCl_3$ solution, in particular in N-H stretching region, clearly reveals the presence of two conformers in those solutions. However in the case of the *Z* isomer there is only one conformer. By referring to the spectra of similar compounds and theoretical calculation it was established that *E* isomer occurs in solution as a mixture of extended conformer and conformer H. As the solvent polarity increases, the participation of the conformer H also increases. Ac-(*Z*)-ΔPhe-NMe_2 adopt in solution exclusively conformer H with amide – phenyl interaction.

Combined theoretical and experimental NMR and IR studies allow to distinguish the *E* and *Z* forms of the studied compounds, predict their ^{1}H and ^{13}C NMR spectra and rationalize their assignment in dilute chloroform solution. Interestingly, the calculated nuclear shieldings (and the recalculated chemical shifts) significantly better reproduced the experimental spectral parameters in the studied compounds than the SSCC parameters.

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Conformational variety and intramolecular tautomerization of mutagenic base analogues: quantum-chemical study

Brovarets O.O., Hovorun D.M.

Department of Molecular and Quantum Biophysics, Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine, 150 Zabolotnoho Str., 03680 Kyiv, Ukraine

Department of Molecular Biology, Biotechnology and Biophysics, Institute of High Technologies, Taras Shevchenko National University of Kyiv, 2 Hlushkova Ave., 03127 Kyiv, Ukraine; E-mails: brovarets@list.ru; dhovorun@imbg.org.ua

A search of elementary physico-chemical mechanisms of spontaneous and induced point mutations of DNA, among which transitions and transversions form a lion's share, is one of central tasks of molecular and quantum biophysics. In this work we aim to find out what new physico-chemical properties must obtain nucleic acid base through its modification to become a mutagene.

As a research object, we chose canonical bases – adenine (Ade), guanine (Gua) and cytosine (Cyt) – and some of the classical mutagens – derivatives of DNA bases, namely 2-aminopurine (2AmPur), 2,6-diaminopurine (2,6-DamPur), hydoxyaminopurine (HamPur), tioguanine (^{6}SGua), N4-aminocytosine (^{4}amCyt), N4-methoxycytosine (^{4}moCyt), N4-hydroxycytosine (^{4}hoCyt), N4-dexydrocytosine (DCyt) and N4-methylcytosine (^{4}meCyt).

We applied for quantum-chemical analysis of conformation properties of monomers and their processes of intramolecular tautomerization density functional theory (DFT) and second-order Møller-Plesset (MP2) predictions using "GAUSSIAN`03" software package.

It is revealed that mutagenic properties of HamPur and ^{6}SGua can be connected with their facilitated ability to transform to the mutagenic tautomeric form in comparison with canonical Ade and Gua bases. However rare mutagenic tautomeric form of bases can inactivates by the turn of purine and its modified analogues accordingly to N1C6 bond in such a way inhibiting their mutagenic activity. At the same time it is necessary to search explanation of 2AmPur and 2,6-DamPur mutagenic activity outside a tautomeric hypothesis, because they demonstrate considerably worst ability to converse to the mutagenic tautomeric form in comparison with Ade.

It is possible to explain the mechanism of mutagenic action of ^{4}amCyt, ^{4}moCyt, ^{4}hoCyt, DCyt and ^{4}meCyt taking into account established by us fact that there mutagenes have more energetically favourable imino tautomeric forms than amino ones. However rare tautomeric forms of Cyt derivatives, believed to have mutagenic properties, can inactivate transforming through two mirror-symmetric transition states to the conformation for which N4H imino group prevents Watson-Crick pairing. This result is not appropriate for DCyt molecule, which modified amino group is fixed.

It is also established that Watson-Crick tautomeric hypothesis can be formally distributed on the investigated molecules so far as lifetime of the their mutagenic tautomers much more exceeds characteristic time which is used by a machinery of DNA biosynthesis on incorporation of one base to the DNA double helix.

Magnetic properties of strongly correlated one-dimensional lattice models of some transition metals complex compounds

V.O. Cheranovskii, E.V. Ezerskaya

V.N.Karazin Kharkov National University

We studied analytically and numerically magnetic properties of three different one-dimensional lattice models described some transition metals complexes. These are decorated spin tube, anisotropic spin delta-chain and ***t-J*** model on necklace ladder.

First one is alternating spin tube structure having three site unit cells. This tube is formed by the folding of stripe fragments of decorated rectangular spin lattice – spin model of real bimetallic ferrimagnets like $\left[\mathrm{Ni(pn)_2}\right]_2\left[\mathrm{Fe(CN)_6}\right]\mathrm{ClO_4}\cdot 2\mathrm{H_2O}$ (pn-1,2 propanediamine). Probably, the corresponding ferrimagnetic nanotubes may be design by lithographic patterning procedures and may be of much interest for modern nanotechnologies – perhaps as magnetic containers for targeted delivery of drugs mediated by external magnetic field.

Above model systems were investigated analytically by means of perturbation theory, spin-wave approximation and numerically by exact diagonalization of the Hamiltonian matrices of small lattice clusters. In order to check the accuracy of our spin-wave analysis, we studied the ground state of infinite cyclic tube fragments by means of DMRG method. We have found that all the ground state energy estimations demonstrate very good agreement. On the base of perturbation theory and exact diagonalization study it was shown that the decorated spin tubes formed by weakly interacted cyclic fragments may demonstrate quantum phase transitions mediated by geometrical frustration. Numerical calculations showed the strong effect of the frustrations on the field dependence of anisotropic spin tubes magnetization at low temperatures which may lead to the appearance of an additional magnetization plateau.

We also studied the energy spectrum and low-temperature thermodynamics of strongly frustrated spin system – delta-chain (or so called saw-tooth chain), describing the magnetic structure of delafossite $YCuO_{2.5}$ and olivines ZnL_2S_4 (L=Er, Tm, Yb). For finite and infinite delta chains with XY coupling in the main chain and different Ising couplings in triangles we obtained analytical solutions for the part of exact energy spectrum. The field dependence of magnetization and temperature dependence of specific heat of the model were calculated on the base of exact energy spectra of finite lattice fragments formed by 4-7 unit cells. The low-temperature intermediate magnetization plateau had been determined at special values of coupling parameters.

Necklace spin ladder describe adequately magnetic structure of complex compound IPA_2CuCL_4 (IPA- isopropylammonium) and some perovskites like $Sr_2Cu_3O_5$. In order to investigate the effects of electron doping on low-temperature thermodynamics and magnetic structure of necklace ladder we used the corresponding ***t-J*** model at different electron fillings. For necklace ladder lattice formed by weakly interacted unit cells we derived effective spin Hamiltonians, described low-energy states of ***t-J*** model. In the case of two electrons per unit cell we found that the low-energy spectrum of the ladder structure formed by “line” cells has no energy gap at small values of spin coupling. In contrast, similar structure formed by “band” cells has energy gap. These effective Hamiltonians were used for detailed study of the low-energy spectrum with emphasis on low-temperature magnetic properties of the model.

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[2] V.O.Cheranovskii, E.V.Ezerskaya, D.J.Klein, A.A.Kravchenko. Magnetic properties of model non-carbon nanotubes with macroscopic value of ground state spin. Journal of Magnetism and Magnetic Materials. 2011, No.323, P.1636-1642.

Anticancer Thiazolidinones Design: Mining of 60-Cell Lines Experimental Data

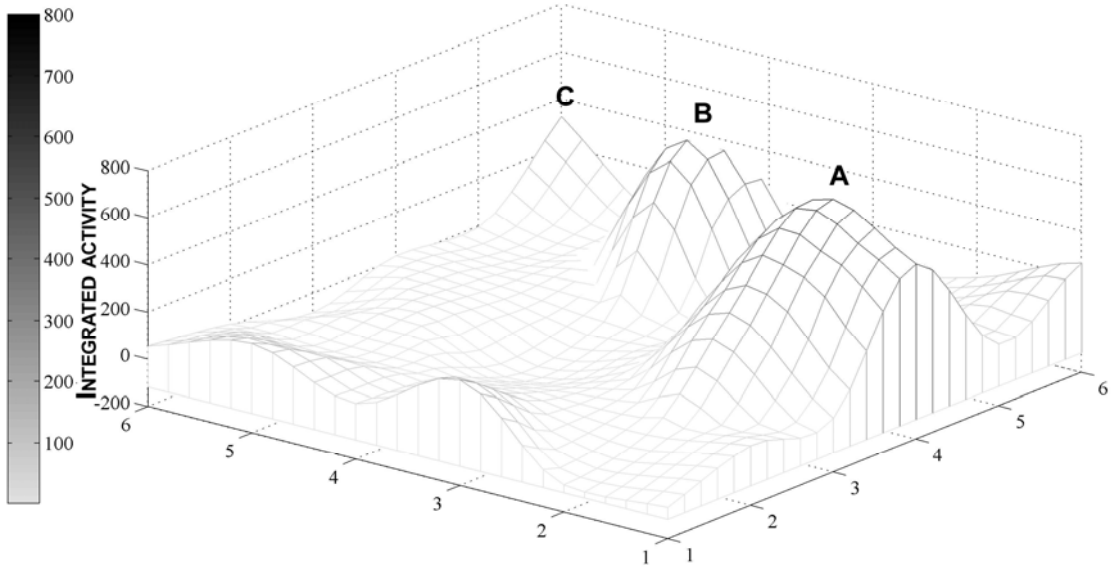
Oleg Devinyak [a], Roman Lesyk [b]

[a] *Uzhgorod National University, Pidgirna 46, 88000, Uzhgorod, Ukraine*

[b] *Danylo Halytsky Lviv National Medical Univeristy, Pekarska 69, 79010 Lviv, Ukraine*

The Developmental Therapeutics Program (DTP) of National Cancer Institute (NCI; USA) provides 60-cell line anticancer screen of supplied compounds with the goal of identifying chemical leads and biological mechanisms. The results of utilizing this screen with novel 4-thiazolidinones formed in-house database. Then, in order to discovery some encapsulated knowledge about anticancer activity mechanism and to create a rational background for further QSAR modelling, data mining was performed. Since DTP 60-cell line screening is a two-stage process, with the first evaluation of all compounds against the 60 cell lines at a single dose of 10 μM and the second evaluation of only active compounds at five doses (including 10 μM), the comparative analysis of both stages results was performed. The aim was to answer: "Has same dose results of this two stages enough statistical similarity to be treated together in future QSAR modelling?" Using Student's *t*-test of residuals it was found, that null-hypothesis about normal distribution of residuals with zero mean is rejected for 41 from 60 cell lines with 5% level of significance. Thus the homogeneity between this two data samples was declined, and further only first stage results were used.

COMPARE-analysis, based on pattern recognition algorithm, showed that studied 4-thiazolidinones activity does not belong to any of well-known anticancer mechanisms. Therefore, Principal Components Analysis and neural network approaches were applied to discover and recognize possible mechanisms of biological action. Using relational sensitivity data, 6×6 Cohonen's Self-Organizing Map was created and trained. The distribution of activities in the neural network gives a possibility to distinguish three classes: two different mechanisms (A and C) and mixed one (B). The similarity and difference in cell lines sensitivities for described mechanisms are pointed.



Since there are three classes of mechanisms, it is necessary to construct three data samples for three QSAR models. Each sample contains active compounds of respective class and all non-active structures. In the other hand, activities of non-active compounds have to be normally distributed with mean growth percent of cancer cells = 100% and unknown variance. Multiple evaluating of *t*-test with slow change of cut-off resulted in the first failure to reject null-hypothesis with minimum growth percent = 86%. Simply saying, all compounds with mean growth percent above 86% have to be treated as non-active. Such introduction of the border between active and non-active compounds let us to form rational data arrays for further QSAR investigations.

Building in silico complex DNA lesions

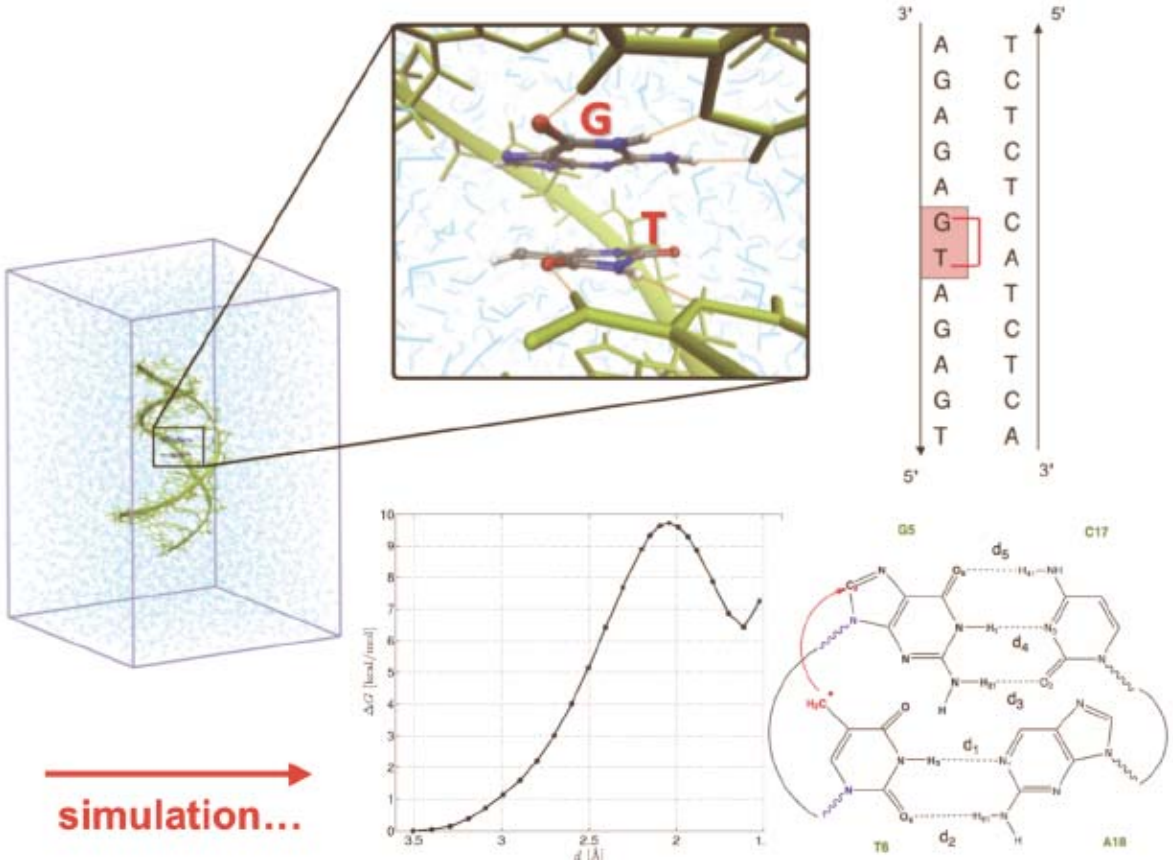
Julian Garrec[a], Chandan Patel[b], Ursula Rothlisberger[a] and Elise Dumont[b]

[a]Laboratory of Computational Chemistry and Biochemistry, BCH 4109, Ecole Polytechnique Fédérale de Lausanne, Suisse

[b]Laboratoire de Chimie, UMR 5182, Ecole Normale Supérieure de Lyon, 46, allée d'Italie, 69364 Lyon Cedex 07, France; e-mail: elise.dumont@ens-lyon.fr

Cellular DNA is continuously exposed to damage reactions, either triggered by exogenenous or endogeneous agents. Around 70 lesions have been experimentally identified so far; a single radical hit, most often an hydroxyle, can initiate a reaction cascade and hence can have a most deleterious action. Most recently, research efforts have been directed towards the structural elucidation of complex tandem DNA lesions, where two nucleobases are covalently tethered. In the case of such statistically rare defects, tandem mass spectrometry most often is the unique analytical tool available. Unfortunately, neither NMR nor DRX structure of an embedded intra- or interstrand cross-link are available, such that information about the structural distortion experencied by the initially regular B-helix are inevitably lost.

We hereby rely on hydrid approaches QM/MM in combination with Car-Parrinello (CP) molecular dynamics with a twofold objective: (i) evaluate an activation free energy and a destabilization cost for a prototypical tandem lesion G[8,5-Me]T and (ii) situate this oxidative ICL compared to other intra-strand adducts (photodefects and cisplatin-bridged) thanks to bend and unwinding angles. The loss of B-helicity turns out to be relatively "shy", which may contribute to explain an altered repair and a high genotoxicity.



In silico fragment-based design of novel anti-inflammatory agents

Olga Filz[a], Athina Geronikaki[b], Dmitry Filimonov[a], Vladimir Poroikov[a]

[a] ***Institute of Biomedical Chemistry of Rus. Acad. Med. Sci., Moscow, 119121, Russia***

[b] ***School of Pharmacy, Department of Pharmaceutical Chemistry, Aristotle University, Thessaloniki, 54124, Greece***

Action on several targets, involved in pathogenesis of complex diseases, can provide an advanced therapeutic effects and a reduced side effects profile in comparison with the action on a selective target.

Design of fragment libraries focused onto the modulation of specific targets can be useful for the search of new multitarget ligands due to the possibility to include fragments or functional groups increasing affinity to a particular target. Currently both *in silico* and *in vitro* methods are applied for design of fragment libraries with specificity to specific target(s).

The main difficulties of such *in silico* methods as docking are small chance to obtain correlation between the calculated and experimental affinity values as well as the problem of true binding pose selection. The main drawbacks of QSAR application to design of fragment libraries are associated with necessity to collect large homogeneous datasets of chemical structures with experimentally determined self-consistent quantitative characteristics of activity.

We propose application of Bayes statistics realized in PASS approach (http://195.178.207.233/PASSonline/) to ligand-based design of fragment library, which can be useful for the design of novel inhibitors of several enzymes having multi-target action. The chemical structure is represented in PASS as a set of Multilevel Neighborhoods of Atoms (MNA-descriptors). MNA-descriptors are calculated iteratively for each atom of the structure using the following rules. The zero-level MNA descriptor is presented as an atom. The descriptor of the first level consists of the atom's zero-level descriptor and zero-level descriptors of its neighboring atoms sorted lexicographically.

The creation of fragment library from structure set is implemented using rules developed on the basis of the data about chemical bond energy. The rules are based on the suggestion that the probability of chemical bond to be broken is inversely proportional to the energy of bond formation.

To obtain the fragments' contribution into the COX-1, COX-2 and LOX inhibition we take into account the mutual influence of atoms included in the considered fragment and their nearest neighbors. Such kind of influence could be estimated using the representation of each atom included in the fragment, as a set of MNA-descriptors up to the 2^{nd} level of MNA descriptors, surrounding considered atom.

The value of fragments' contribution is obtained as an average value of atom's contributions. Fragments' contribution value is then normalized using the occurrence frequency obtained for each fragment among the sets of active and inactive compounds. Therefore fragments' contribution is obtained on the basis of each atom's contribution (before chemical structure is splitted into fragments) and *a priori* estimation of fragments' occurrence in the sets of active and inactive structures.

The method was applied to design of new anti-inflammatory agents, inhibitors of cycloxygenase-1 (COX-1), cycloxygenase-2 (COX-2) and lipoxygenase (LOX).

Using calculated contribution values and taking into account synthetic accessibility of compounds which can be designed based on prepared library, we selected set of fragments which were incorporated in the set of promising COX-1,2 and LOX inhibitors. The selected fragments included: benzothiazole, benzol, phenol, fluorobenzene, chlorobenzene, anisole and 2-imino-5-methylidene-1,3-thiazolidin-4-one. Increasing of affinity values in *de-novo* designed compounds were found in comparison with earlier designed inhibitors, including thiazole derivatives.

Therefore, the suggested method of fragment library preparation provides selection of fragments that can be used for the design of potent multitarget agents.

Constrained optimized potential method for excited states

V.N. Glushkov

Dept. of Physics, Electronics and Computer Systems, Dnepropetrovsk National University, Ukraine; e-mail: v_n_glushkov@yahoo.com

It is known that a combination of density functional theory (DFT) and optimized effective potential (OEP) methodologies can be considered as the undisputed workhorse of modern electronic structure ***ground state*** calculations. Nevertheless, this research area for ***excited states*** (ES) is as yet not clearly understood. Nowadays, there are scarce DFT calculations for excited states and, in particular, based on the OEP methodology, especially for ESs, having the same symmetry as the ground state.

In this talk a constrained variational approach based on an asymptotic projection (AP) method and its applications to the OEP problem for excited states is reviewed. The basic tenets of a simple to implement AP method for taking the necessary orthogonality constraints into account are presented. Amended one-particle Schrödinger equations with a multiplicative potential are derived to determine orbitals of singly [1, 2] and doubly [3] excited states having the same spatial and spin symmetry as the ground state. The Slater determinant for a given excited state constructed from the orbitals is orthogonal to one-determinantal functions of low-lying states. The corresponding excited state OEP equations determining parameters of a local potential expressed in terms of the external potential are obtained and analyzed. A general procedure for application of the constrained OEP method to excited state problems is demonstrated by means of practical excited state calculations for simple atoms and molecules at different levels of approximation including both exchange-only results and exchange-only + correlation studies. Practical calculations have showed that a simple to implement COEP methodology is capable of delivering fairly accurate results on the energies of singly and doubly excited states and can be easily applied to both atoms and molecules.

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Prediction of Adsorption Gibbs Free Energy at M05-2X DFT Level of Theory: an Interaction of Nitro-Compounds with a Surface of Carbon

L. Gorb,[a] A. Michalkova,[b] F. Hill,[b] J. Leszczynski[b,c]

[a]*Badger Technical Services, LLC, Vicksburg, Mississippi, USA*

[b]*U. S. Army Engineer Research and Development Center (ERDC), Vicksburg, Mississippi, USA*

[c]*Interdisciplinary Nanotoxicity Center, Department of Chemistry and Biochemistry, Jackson State University, 1400 Lynch Street, P. O. Box 17910, Jackson, MS 39217, USA*

The details about the structure and interactions of benzene, polycyclic aromatic hydrocarbons and aromatic nitrocompounds with a carbon surface modeled by coronene using a density functional theory approach along with the M05-2X functional will be provided. The adsorption was studied in vacuum and from water solution. The molecules studied are physisorbed on the carbon surface. While the intermolecular interactions of benzene and hydrocarbons are governed by dispersion forces, nitrocompounds are adsorbed also due to quite strong electrostatic interactions with all types of carbon surfaces. Based on these results, we concluded that the method of prediction presented in this study allows one to approach the experimental level of accuracy in predicting thermodynamic parameters of adsorption on a carbon surface from the gas phase. The empirical modification of the polarized continuum model leads also to a quantitative agreement with the experimental data for the adsorption Gibbs free energy values from water solution.

Confinement effect on *p*-nitroaniline properties

Anna Kaczmarek–Kedziera

Faculty of Chemistry, Nicolaus Copernicus University, Gagarina 7, 87–100 Torun, Poland; Email: teoadk@chem.umk.pl

An analysis of the behaviour of the *p*-nitroaniline in confinement is performed. Various confining enviroments are chosen to demonstrate the chemical pressure exerted by a homogeneous cylindrical structure (single–walled carbon (4,4) nanotube), a heterogeneous cylindrical structure (boron–nitride (4,4) nanotube) and a spheroidal homogeneous structure (C_{92} fullerene buckyball of the original D_2 symmetry). The highest interaction energy was found for pNA in the carbonaceous cages, however its estimation must be performed with a careful choice of the approximation. Boron–nitride tube with the relatively large band gap appears to be an interesting environment modifying the electronic spectrum of pNA.

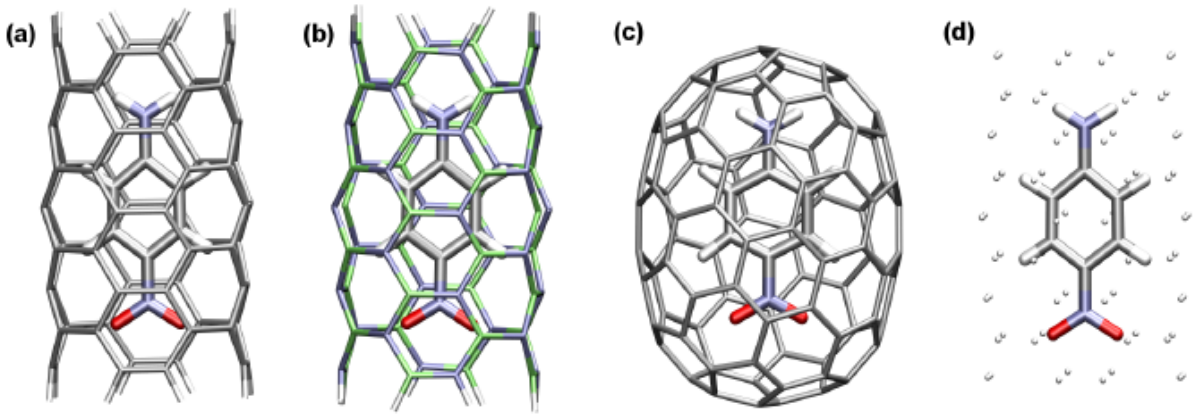


Figure 1: Endohedral complexes investigated in the present study: (a) pNA in carbon (4,4) nanotube, (b) pNA in boron-nitride (4,4) nanotube, (c) pNA in C92 fullerene, (d) pNA in helium (4,4)-like nanotube

Modeling the interaction of molecular and radical particles with surface of carbonaceous clusters

M.T. Kartel, V.S. Kouts, E.M. Dem'yanenko, K.V. Voitko, O.M. Bakalinska

Chuiko Institute of Surface Chemistry, NAS of Ukraine, General Naumov str. 17, Kiev 03164, Ukraine

Recently there has been significant progress in creating functional materials based on carbon (active carbons, exfoliated graphite, nanotubes, fullerenes, graphene etc.) for adsorption, catalytic and electrochemical processes as well as for medical application. Analysis of literature data shows that the introduction of heteroatom nitrogen and oxygen into carbon matrix can change its donor-acceptor ability and correspondingly catalytic, absorption, electrochemical and biospecific properties of carbon materials.

This paper considers simulation of two processes: a) catalytic decay of hydrogen peroxide (H_2O_2) on activated carbon and b) the interaction of nitroxyl radical (spin probe) with carbon nanotubes.

It is known that the reaction of hydrogen peroxide decay is a complex chain process, where the limiting stage is the disintegration of a molecule of hydrogen peroxide on two hydroxyl radicals •OH. We assume that catalytic effect of graphite plane defines by shifting equilibrium of initial H_2O_2 decay process towards the formation of •OH radicals due to chemisorption of the last on the carbon surface.

As the models of graphite planes of active carbon (AC), oxidized carbon (AC_O) and nitrogen-containing carbon (AC_N) were selected clusters $C_{42}H_{16}$, $C_{45}O_5H_{16}$, $C_{40}N_2H_{16}$ and boron-containing cluster $C_{40}B_2H_{16}$ (contents of boron and nitrogen in clusters $C_{40}A_2H_{16}$ are ~4.5 at% relatively C-atoms, and oxygen in $C_{45}O_5H_{16}$ is ~13 at%). The aim of this work was to establish the thermodynamic and kinetic characteristics of the interaction of •OH with graphite planes. Calculations were carried out by *B3LYP/3-21G (d.p.)* method. The interaction of graphite planes with radicals occurs through the formation of physically adsorbed complex and the formation of chemical bonds between the reactants after overcoming the energy barrier. It is found at physical adsorption complex [C-cluster... •OH] formed, and •OH radical coordinated with the graphite plane through H- atom, while in activated complex •OH radical was parallel to plane of cluster. Electron density is transferred from the π-system of the carbon matrix into radical. The values of energy of physical adsorption, energy of activation (energy barrier of H_2O_2 decomposition) and charge transfer correlated with electron donor ability of clusters. The obtained results are confirmed by experimental data of rate constants, $k*10^4$ c^{-1} for reactions of hydrogen peroxide decomposition in the presence of carbon materials AC, AC_O and AC_N.

To study the mechanism for cytotoxicity (integrity of erythrocytes membranes and activity of hepatocytes mitochondria) on the molecular level it is used spin probe method (nitroxyl radicals, NR). It is shown the mechanism of CNT toxicity is due to destruction of cytoplasmatic membrane and inhibition of respiratory chain of mitochondria. In this research by methods of electron paramagnetic resonance (EPR, *Bruker ELEXSYS E580 FT/CW, X-band*) and quantum chemistry (*UHF/3-21G, Gaussian 03*) it is investigated the systems: high-purity multiwall carbon nanotubes (CNT), spin probe as well as spin-labeled CNT. EPR-spectra of suspensions "CNT+NR" and spin-labeled by NR CNT in solution is superposition of spectra, from at least two radicals with isotropic slow and fast rotation movement. Quantum-chemical calculations demonstrate that superfine interaction constants (a^N) and spin density (ρ^N_s) on nitrogen nuclear of NR (as are inside and outer CNT) are almost identical and coincide with the experimental values. In sorption complexes CNT...NR and on spin-labeled CNT there are arising spin density on CNT, joining molecular orbitals of CNT and NR, and electronic density is transferring from CNT on NR.

Complexation of ibuprofen, declofenac and insulin with low molecular weight chitosan

Khaldoun Al-Sou'od

Department of Chemistry, Faculty of Science, Al al-Bayt University, P.O. Box 130040, Mafraq 25113, Jordan

The complexation between ibuprofen, declofenac and insulin with the low molecular weight chitosan (LMWC) was studied using molecular modeling method. Molecular mechanics (MM) calculations were used to have insight into interaction stiochiometry between chitosan and ibuprofen. The results of MM showed that the complexation of ibuprofen with LMWC involves ionic interaction between the ammonium group of LMWC and the carboxylate anion of ibuprofen. Chitosan was built in two different forms. The long one practically can be obtained from diluted solutions while the short one are from concentrated solutions. The modeling show that the chitosan…ibuprofen complex is best prepared from diluted solutions of the chitosan polymer.

Human Insulin is also build using a hyperchem software. It is a rather small protein, with a molecular weight of about 6000 Daltons. It is composed of two chains (A and B) held together by disulfide bonds. The interaction between human insulin and LMWC was studied using MM calculations.

Antiferromagnetic ordering in the conjugated chains of disordered postoplymeric carbon: a case DFT investigation

Oleksiy V. Khavryuchenko,[a,c] Volodymyr D. Khavryuchenko,[b] Gilles H. Peslherbe[c]

[a] *Chemical Department, Kyiv National Taras Shevchenko University, 64 Volodymyrska str., UA-01601, Kyiv, Ukraine*

[b] *Institute for Sorption and Problems of Endoecology, National Academy of Sciences of Ukraine, 13 General Naumov str., UA-03167, Kyiv, Ukraine*

[c] *Centre for Research in Molecular Modeling and Department of Chemistry and Biochemistry, Concordia University, Montréal, QC, Canada H4B1R6*

Establishing a comprehensive model of ACs and computing their properties is an intense area of research due to the wide application of carbon materials and their practical importance. However, the majority of such models are still based solely on ordered graphite-like clusters or non-bonded curved carbon sheets. Another aspect of the AC chemistry, which is often overlooked, is the dependence of the chemical and physical properties of the material under consideration on its spin state (i.e. multiplicity). In this work, we report and discuss the results of density-functional theory calculations of the electronic structure and spin properties of both graphite-like and disordered carbon clusters, as models of the postulated two major domains of AC.

Spatial structure of the amorphous domain cluster has been constructed from a series of different polymer-precursors models by simulation of carbonization through stepwise elimination of hydrogens and subsequent optimization of the geometry in different multiplicity states. The final geometry, being unique, is taken as an arbitrary model for a disordered amorphous domain as the one, representing typical statistic distribution of properties.

The electronic structure of model clusters of the graphite-like and disordered amorphous domains of active carbon has been calculated with density-functional theory (B3LYP/SVP). Structural transformations of amorphous clusters are observed upon change of multiplicity, and high-multiplicity states are found to be the most stable. Spin-active centres tend to form conjugated chains with an electronic structure made up of non-interacting singly-occupied orbitals.

Spin contamination extent is analyzed for the models in different multiplicity states. The essence of spin contamination as a measure of antiferromagnetic ordering of weakly spin centres is discussed and compared to results by complete active space SCF (CASSCF) methodology.

Generative Topographic Maps (GTM) as a universal tool for data visualization, predicting activity profiles and comparison of databases

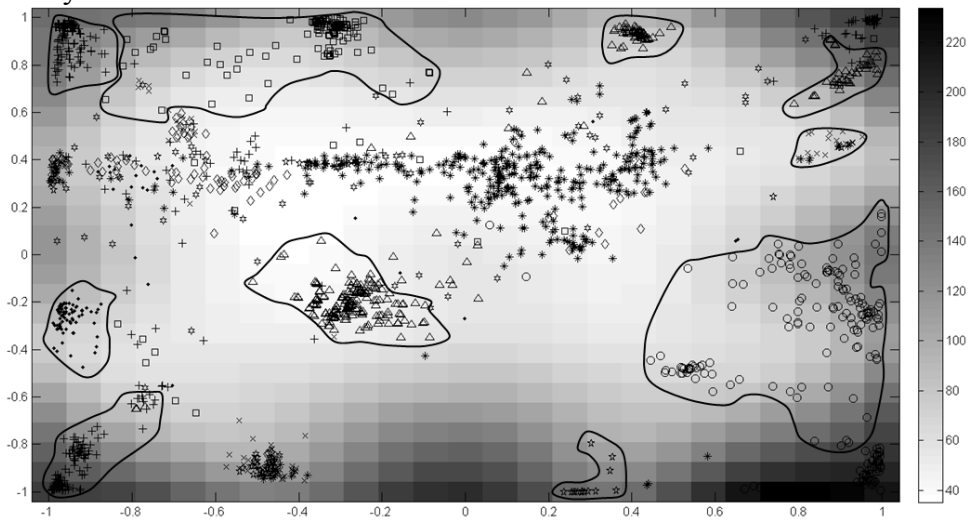
N. Kireeva [a,c], I.I. Baskin[a,b] and A. Varnek[a]

[a] *Laboratoire d'Infochimie, UMR 7177 CNRS, Université de Strasbourg, 4 rue B. Pascal, Strasbourg 67000, France*

[b] *Department of Chemistry, Moscow State University, 119991, Moscow, Russian Federation*

[c] *Institute of Physical Chemistry and Electrochemistry RAS, Leninsky pr-t 31, 119991 Moscow, Russian Federation*

This presentation concerns Generative Topographic Maps (GTM) [1] which is an universal tool to visualize the chemical space, to predict activity profiles, to conduct virtual screening and to compare databases of chemical compounds. Unlike other popular methods of data visualization (Principal Component Analysis, Self-Organizing Maps (SOM), etc), for a given molecule GTM calculates its probability to be located in the given point of rectangular 2D map. Thus, for a whole dataset GTM not only visualizes the data points, but calculates the probability density function. In turn, this allows one to calculate an overlap between two datasets and to prepare classification models if information about activities of compounds is available. The model calculations performed on the DUD dataset [2] using ISIDA SMF [3], ISIDA IPLF [4], Fuzzy Pharmacophore Triplets [5] and MOE 2D [6] descriptors illustrate the utility of GTM.



Generative Topography Map for the dataset of the DUD ligands against 10 different biological targets. The background color code corresponds to "magnification factor" which relates the distances between the objects in the initial descriptors space with those on the map.

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Using QSPR methodology for accurate prediction of temperature related aqueous solubility of nitro-compounds

Ognichenko L.N.[a], Klimenko K.A.[b], Gorb L.[c], Hill F.C.[d], Kuz'min V.E.[a], Polishchuk P.G. [a], Artemenko A.G.[a], Leszczynski J.[d,e]

[a] *Laboratory of Theoretical Chemistry, Department of Molecular Structure, A.V. Bogatsky Physical-Chemical Institute National Academy of Sciences of Ukraine, Lustdorfskaya Doroga 86, Odessa 65080, Ukraine; e-mail: ognichenko@mail.ru*

[b] *I. I. Mechnikov National University, Dvorianskaya 2, Odessa 65026, Ukraine*

[c] *Badger Technical Services, LLC, Vicksburg, Mississippi, USA*

[d] *U. S. Army Engineer Research and Development Center (ERDC), Vicksburg, Mississippi, USA*

[e] *Interdisciplinary Center for Nanotoxicity, Department of Chemistry, Jackson State University, Jackson, Mississippi, 39217, USA*

Information on the solubility of new and emerging compounds is an important factor for environmental risk assessment, providing data for the modeling of transport and fate of chemical compounds and for understanding the pharmacokinetic behavior of contaminants in living organisms. The manufacturing, storage, transportation and utilization of munitions can lead to the release of nitro- and nitroso-compounds into the environment. These compounds and their metabolites may have long-term environmental impact. In many cases aqueous solubility (S_w) of new and emerging chemicals is the determinative property for the estimation of the environmental impact of these compounds and drives research related to remediation techniques. However, S_w experimental data, particularly on military crucial contaminants, often are not available and in most cases are only available as predicted values based on existing QSPR methodologies.

Considering the fact that solids' and liquids' water solubility depends on temperature, this study for the first time attempting to describe such relationship via QSPR methodology. Solubility data were taken from Handbook of aqueous solubility data [1]. Molecular descriptors calculation was carried out using 2D-QSPR approach based on simplex representation of molecular structure. Simplex vertexes were differentiated by atom type, refraction, lipophilicity, partial atomic charges, refraction and the ability for an atom to be a donor or acceptor in hydrogen bond formation.

QSPR models were created using PLS and Random Forest [2] approaches. Obtained models, which describe structure-property relationships, have good statistical characteristics. Furthermore, a novel approach was applied that resulted in development of a model which includes temperature as a parameter.

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Quantum-chemical study of adhesion contact of heterogeneous metals in corrosive environment

V. Pokhmurskii, V. Kopylets

Karpenko Physico-Mechanical Institute of the National Academy of Sciences of Ukraine, 5, Naukowa Str., 79060 Lviv, Ukraine; e-mail: E-mail: pokhmurs@ipm.lviv.ua

Highly symmetrical cubo-octahedral clusters of Al, Cu, Fe, Cr has been simulated as possible widely used metals in the study of tribology and contact processes of practical interest. The main energetical behavior was surface energy and the following original procedure suggested: total energy of homogeneous clusters Me_{55} and Me_{59} were calculated with geometry optimization for each type of metal, then the formed clusters were separated into two asymmetrical fragments at a distance of 0.6 nm and each structure was optimized for the atomic positions of surface fragments, involved to the future contact zone. Rest of the structures was frozen for each fragment.

By means of quantum-chemical semiempirical PM6 (MOPAC 2009 [1]) calculation we studied a contact interaction of two clusters, obtained from a symmetrical cross-cut separation of original geometry optimized stable clusters Al_{55}, Cu_{55} (f.c.c) and Fe_{59}, Cr_{59} (v.c.c.) in vacuum and a model corrosive environment.

During their interaction surface energy in a strongly proportional way was transferred into adhesion energy for the contact zone as much as a half of its initial value.

Two energy minima with two saddle points of activation energies were calculated during potential energy curve scanning. The deepest minimum corresponded to the formation of usual metallic bonds (a reverse process to cluster separation) in the conjugated clusters, while the second one was caused by a quasi-chemical bonding in resemblance with an intermediate state, formed by physical and (partly) chemical adsorption of two interacting surfaces. Such a state was influenced by our environment – water molecules exclusively and water molecules with chloride ions. The influence of the environment was quit opposite to that of strong metallic bond formation.

Cluster pairs $Al_{33} – Al_{22}$, $Fe_{38} – Fe_{21}$, $Cr_{38} – Cr_{21}$, $Al_{33} – Fe_{38}$, $Al_{33} – Cr_{38}$, $Cu_{33} – Al_{33}$, $Cu_{33} – Fe_{38}$ showed a stable growth of adhesion energy by 20 – 30 % in the presence of water and 40 – 300 % in the presence of water and chloride ions. This discrepancy may be induced by a synergetic effect of common action of H_2O and Cl^- in accordance with experimental observation.

Surface energies for our contacting surface indexes (111) were in the values of one order with other studies (as an example – for Al surface energy 5.68 eV/nm^2 in DFT LDA approximation and 4.68 eV/nm^2 in DFT PBE calculation and experimental values [2] 7.12 eV/nm^2). Our value for Al was 5.13 eV/nm^2 in vacuum.

The results of this work may contribute to atomic mechanism explanation of the initial stages of processes and phenomena of chemical and electrochemical tribocorrosion of constructive metals in natural and industrial aggressive environments.

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Using the kernel-methods for solving the «structure-property» task

A.V. Bekker, G.N. Apryshko, M.I. Kumskov

MSU named after M.V. Lomonosov, Institute of Experimental Diagnosis RCRC named after N.N. Blohin RAMS

The task of finding the functional dependence of the biological activity of chemical compounds (task «structure-property», QSAR-problem [1]) is an important task of mathematical chemistry, the solution of which allows the synthesis of chemical compounds with certain desired properties without the expense of time and tools.

The aim is to construct efficient algorithms for constructing models to predict the biological activity of chemical compounds, evaluation of predictive ability of these models in specific samples of chemical compounds.

The most common algorithms for solving the «structure-property» task is a description of the objects of the training sample in the form of vectors of descriptors [2] and the search for functional relationship between attributes of the object and its "external" property - the activity. With this algorithm, training sample is represented as a matrix of "molecule-descriptor" to which you can use standard algorithms for pattern recognition. However, the solution of such an algorithm associated with a number of difficulties related to large-dimensional matrix "molecule descriptor" and the need to select the most informative descriptors.

The paper proposes an alternative approach to solving the problem based on the use of kernel-functions [3] allows to describe not the objects themselves but the relationship between the objects or the measure of their similarity. Kernel-functions are symmetric functions with the number of constraints. As a result of this algorithm after description all the information about the training sample needed to further build the model is contained in a symmetric square matrix with dimension equal to the dimension of the training sample. Next to the resulting matrix can be used kernel-modification of different algorithms of data analysis such as principal component analysis, a method of support vector machines, clustering algorithms, and others.

This paper investigates the applicability of the «kernel-methods» to the description of chemical compounds to find the «structure-property» dependence. The computational experiments carried out on samples of chemical compounds, in particular, derivatives of betulin molecules that exhibit anticancer activity in the experiment. Structural formulas and data on the presence or absence of activity of substances extracted from the databases of anticancer agents of the Russian Cancer Research Center named after N.N. Blohin RAMS.

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Complete basis set limit (CBS) prediction of accurate NMR parameters

Teobald Kupka[a], Michał Stachów[a], Marzena Nieradka[a], Tadeusz Pluta[b], Jakub Kaminsky[c], Stephan P. A. Sauer[d]

[a]*University of Opole, Faculty of Chemistry, Opole, Poland; Institute of Chemistry*

[b]*University of Silesia, 40-007 Katowice, Poland*

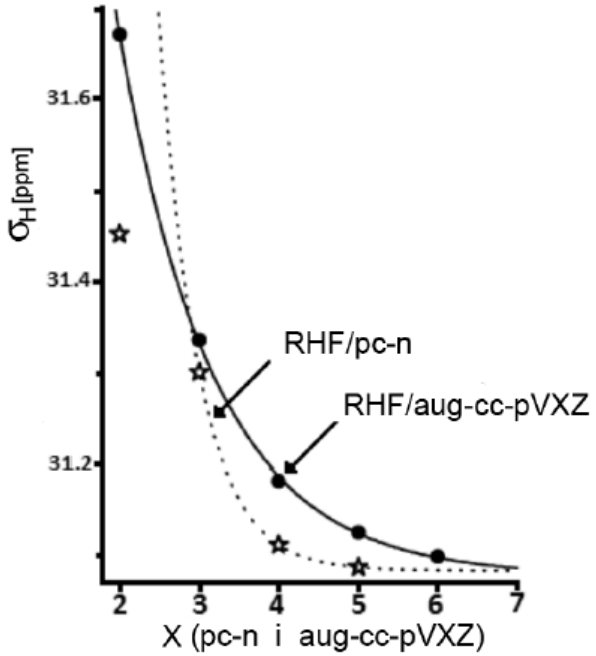
[c]*Department of Molecular Spectroscopy, Institute of Organic Chemistry and Biochemistry, 166 10 Prague, Czech Republic*

[d]*Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark*

Theoretical calculations of NMR parameters (nuclear isotropic shieldings and indirect spin-spin coupling constants) are widely used to support experimental studies. The accuracy of calculated parameters depends on the inclusion of correlation effect, method of calculation, size and flexibility of the basis set, intermolecular interactions, temperature, as well as on corrections due to molecular rovibrations.

The idea of estimating theoretical NMR parameters (nuclear shieldings and indirect spin-spin coupling constants) toward the complete basis set limit (CBS), in analogy to predicting reliable thermochemical data of chemical accuracy, will be discussed. The use of Dunning's correlation-consistent, Jensen's polarization-consistent and Jorge XZP basis set families for calculation on NMR parameters of selected model molecules at RHF, MP2, DFT and CCSD(T) level will be illustrated.

The convergence of proton isotropic nuclear magnetic shielding of water, calculated using pc-n and aug-cc-pVXZ basis sets is shown below. The continuous lines represent three-parameter fits toward the complete basis set limit.



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Spin-orbit coupling in the $Ir(ppy)_3$ and in the Pt-porphyrin complexes calculated by density functional theory and studied with the phosphorescent microwave double resonanse

B. Minaev[a], S. Perumal[b], O. Vahtras[b], V. Minaeva[a], and H. Agren[b]

[a]*Institute of Natural Sciences, Bohdan Khmelnitskii National University of Cherkassy, bvd. Shevchenko 81, 18031 Cherkassy, Ukraine; E-mail: bfmin@rambler.ru*

[b]*Department of Biotechnology, Royal Institute of Technology, 10691 Stockholm, Sweden*

The photo-physical properties of Ir(III) and Pt(II) complexes have been studied by a wide variety of spectroscopic techniques [1,2] including theoretical interpretation as well [3-6]. Strong spin-orbit coupling (SOC) at the Ir(III) centre provides an efficient phosphorescence of such species and relatively high zero-field splitting (ZFS) of the lowest triplet state. The cyclometalated tris-phenylpyridine-Ir(III) complex [1] and its derivatives [2] have been used in organic light-emitted diodes to overcome the efficiency limit imposed by spin dependence of light emission during electron-hole recombination and formation of triplet excitons. Thus their phosphorescence has been studied in a number of works [1-4] including a special attention to ZFS spin sublevels selectivity and spintronics [3,4]. In low-temperatures crystals of the $Ir(ppy)_3$ complex the phosphorescence has been modulated by applied magnetic field and by temperature variations [1]. Tentative interpretation of these spin-dependent effects has been presented on the ground of DFT calculations of ZFS and spin-sublevels selectivity [3-5].

In this presentation we discuss our simulation of the possible phosphorescent microwave double resonance (PMDR) experiment for the $Ir(ppy)_3$ complex. Since ZFS-transition energies are comparable with low-frequency vibrations (including C-Ir-N and intermolecular modes), some unusual resonances and vibronic effects are predicted which could be used in spintronic devices.

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Molecular dynamics of proteins: optimal criteria for reliable trajectories

A.Yu. Nyporko

Taras Shevchenko Kiev National University, High Technology Institute, Kiev, Ukraine; e-mail: dfnalex@gmail.com

Molecular dynamics computation is very useful method for investigation of protein structure [1]. This approach gives a possibility to discriminate and evaluate the nuances of protein structure and behavior which are indiscernible for other methods (in particular, distant correlative motions [2] and distant effects of amino acid replacements [3,4]) as well as allow to observe perturbations of protein structure for some of time. However, despite usability and wide facilities, results obtained via molecular dynamics sometimes are ambiguous. Main claim to molecular dynamics is the slow but stable gradual increase of protein oscillation amplitude and, as a result, lack of relaxation of molecular system that is observed in some cases. Thus, the aim of this research is selection of optimal criteria for molecular dynamics calculations (force fields, calculation parameters, etc.) to generate time-stable protein motions trajectories which correlate with NMR-derived motions' patterns.

Protein Data Bank was scanned to retrieve the spatial structures of water-soluble proteins, participating in cytoskeleton functioning, which are resolved by NMR spectroscopy and have no less than 20 deposed conformers. Among them the four proteins were selected in a random way for 50 ns molecular dynamics calculation with various criteria/conditions (PDB access codes are 1UNC, 1AJ3, 1GM1 and 1T0Y). Calculations were carried out with GROMACS 4.0.3 software using force fields Gromos 96, Gromacs and OPLS. The next parameters were varied: *nstlist* – frequency to update the neighbor list (0, 1, 10, 100), *comm_mode* – center of mass motion removal function (none, linear, angular), *T-coupling* – thermostat function (berendsen, V-rescale), *rcoulomb* – computation method for electrostatic interactions (cut-off, PME). Structural stability was estimated by conformational energy dynamics (using *g_energy* module), and levels of molecular oscillations (using *g_rms* module). Motion patterns for each studied protein were obtained from 20 molecular dynamics' conformers with lowest potential energies and compared with appropriated patterns calculated from NMR-derived conformers.

Among studied parameters of molecular dynamics calculations PME method of electrostatic interactions evaluations shown the most stabilize effect on protein dynamics. Application of this method in combination with any others resulted in stable horizontal plateau of molecular oscillations and decrease of average oscillation level and oscillation amplitude. Using V-rescale thermostat resulted in accelerated stabilization of motions level. Variation of *nstlist* hasn't produced significant consequences (except nstlist=1 resulted in accelerated stabilization of system similar to V-rescale action). Effects of center of mass motion removal function were ambiguous. Among studied force fields OPLS appeared to be the most optimal for molecular dynamics calculations. Profiles of oscillations of individual amino acid residues obtained from trajectories calculated with OPLS are similar to NMR motion patterns for all studied protein. Using Gromacs force field revealed good correlation with NMR data for 1GM1 and 1T0Y proteins, using Gromos 96 force field – with NMR data for 1T0Y only. Thus, application of OPLS force field with PME electrostatic calculation and V-rescale thermostat seems to be optimal for molecular dynamics calculation and gives a possibility to obtain the protein dynamics trajectories comparable by a quality with NMR data.

[1] M. Meli, G. Colombo (2009) Molecular simulations of peptides: a useful tool for the development of new drugs and for the study of molecular recognition. *Methods Mol Biol,* **570**:77-153.

[2] O. F. Lange, H. Grubmaller (2008) Full correlation analysis of conformational protein dynamics. *Proteins,***70***:*1294-312.

[3] P. Lazar et al. (2009) Molecular modeling study on the effect of residues distant from the nucleotide-binding portion on RNA binding in *Staphylococcus aureus* Hfq. *J Mol Graph Model.* **28**:253-260.

[4] A.Yu. Nyporko, Ya.B. Blume (2008) Influence of amino acid replacements associated with multidrug resistance on β-tubulin molecular dynamics. (The Sixth Intl. Conference on Bioinformatics of Genome Regulation and Structure (Novosibirsk, Russia, June 22-28, 2008). Book of Abstracts, Novosibirsk, 2008, p. 177.

New QSPR equations for accurate prediction of octanol-water partition coefficient for organic compounds

L.N. Ognichenko[a], V.E. Kuz'min[a], L. Gorb[b], F.C. Hill[c], P.G. Polischuk[a], A.G. Artemenko[a], J. Leszczynski[c,d]

[a] *Laboratory of Theoretical Cmemistry, Department of Molecular Structure, A.V. Bogatsky Physico-Chemical Institute of the National Academy of Science of Ukraine, Ukraine, Odessa, 65080, Lustdorfskaya Doroga 86; e-mail: ognichenko@mail.ru*

[b] *Badger Technical Services, LLC, Vicksburg, Mississippi, USA*

[c] *U. S. Army Engineer Research and Development Center (ERDC), Vicksburg, Mississippi, USA*

[d] *Interdisciplinary Center for Nanotoxicity, Department of Chemistry and Biochemistry, Jackson State University, Jackson, Mississippi, 39217, USA*

Lipophilicity plays a key role in many biochemical, pharmacological and ecological processes. The octanol-water partition coefficient ($LogK_{ow}$) is widely applied in quantitative structure – activity/property relationship (QSAR/QSPR) studies. This property is used to provide invaluable information for overall understanding of the absorption, distribution, metabolism and elimination of a wide variety of chemicals. However, experimental estimation of $LogK_{ow}$ is expensive. Thus, there is a need to have reliable computational method that can be used for accurate prediction of lipophilicity for chemical compounds based on their structures. Currently, most of the existing theoretical methods for the calculation of $LogK_{ow}$ are based on the assumption that the properties of a molecule could be represented as a sum of the properties of its structural fragments. In reality, lipophilicity does not obey the additive scheme. Some of the existing methods need experimental correction factors. This is the reason why the accuracy of such predictions using different QSPR methods is frequently unacceptably low for estimations of physical characteristics, including $LogK_{ow}$.

In this work Simplex Representation of Molecular Structure (SiRMS) [1] in combination with the Random Forest (RF) method [2] is used for the estimation of fragment contributions to lipophilicity in a non-linear manner.

Experimental values for $LogK_{ow}$ were obtained from the PHYSPROP database (version 2004) containing 13474 compounds. After removing compounds containing salts, mixtures of molecules, erroneous or wrong structures and duplicates a total number of 10973 compounds, having experimental $LogK_{ow}$ values, were selected for the data set. $LogK_{ow}$ values varied from -5.08 to 11.29, with an average value of 2.14.

Accurate "structure - $LogK_{ow}$" 2D QSPR model based on SiRMS approach and RF statistical model has been developed for a set of more than 10970 organic compounds and has been successfully validated with two external test sets. Importance of descriptors was estimated, physico-chemical factors influencing on lipophilicity were determined. The developed model predicts the $LogK_{ow}$ values at the level of the best modern models. $LogK_{ow}$ values of 29 military important compounds with unknown experimental value of $LogK_{ow}$ have been predicted.

[1] Kuz'min V.E., Artemenko A.G., Polischuk P.G. et al.//J.Mol.Model.-2005.-11.- P.457-467.
[2] Polishchuk P.G., Muratov E.N., Artemenko A.G. et al. // Chem. Inf. Model.- 2009.- V. 49. - P. 2481-2488.

Interpretation of QSAR models based on Random Forest method

P. Polishchuk, A. Artemenko, V. Kuz'min

A.V. Bogatsky Physical-Chemical Institute NAS of Ukraine, Odessa, Ukraine

There are five principles approved by OECD for development of QSAR models. One of them is interpretability of the models. QSAR models based on Random Forest method meet all these requirements except the last one. Now only one way to explore the "black box" of Random Forest models is available – estimation of variables importances. This procedure is rather time-consuming and obtaining information is often insufficient for understanding how structure influences an activity.

We propose new procedure for interpretation of Random Forest models. It allows to estimate contribution of each descriptors to investigated property. Contributions of descriptors calculate separately for all compounds so the main feature of the approach is dependence of descriptors contributions on the molecular surroundings. First, mean activity values among training set compounds which fell the nodes are calculated in each node of each tree in the forest. The differences between these values in the current node and the parent one is considered as a contribution increment of the descriptor of the current node to the property. For each compound all contributions of corresponding descriptors, which are in the nodes containing this compound, are summarized and divided on the number of trees in the forest.

In the case of simplex representation of molecular structure it is possible to calculate atoms contributions from the contributions of separate simplex descriptors (tetraatomic molecular fragments). It allows to clearly interpret influence of structure on an activity. Obtained information is also valuable for design of new compounds with predefined activity level.

To validate of the proposed approach a single QSAR task for the set of ligands of serotonin 5-HT_{1A} receptors were solved by means of Random Forest method and PLS, which has univocal interpretation. Descriptors contributions were calculated for each model and contributions in the affinity for 5-HT_{1A} receptors of separate molecular fragments were estimated. Found regularities of structure-activity relationships were almost the same for the both models. The second evidence of the reliability of the proposed approach was comparison of absolute values of calculated descriptors contributions with descriptors importances estimated by the procedure proposed by Breiman. As it can be expected the more important descriptors will have bigger absolute contribution values. The subsequent analysis revealed good correlation between these parameters, $R_{Spearman} = 0.88$.

Island charge distribution in the W-shaped 2,3,4-triphosphapentadienyl derivatives and related compounds

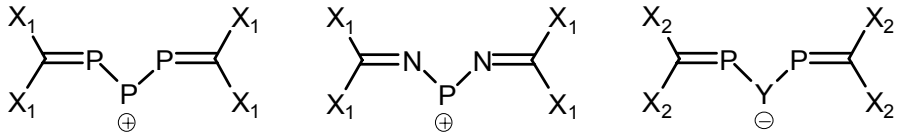
A. B. Rozhenko [a,b], L.V. Zozulya [a], W.W. Schoeller [b,c]

[a] ***Institute of Organic Chemistry, Murmans'ka str. 5, 02660, Kyiv, Ukraine***

[b] ***Fakultät für Chemie der Universität Bielefeld, Postfach 10 01 31, 33501 Bielefeld, Germany***

[c] ***Department of Chemistry, University of California, Riverside, CA 92521-0403, USA***

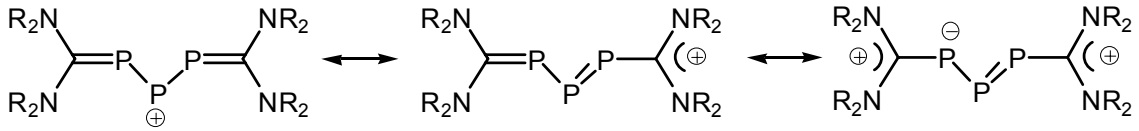
The anionic and cationic structures **1-3** involving the P-P-P triad and As and SB homologues **4,5** have been investigated at the DFT and MP2 levels of theory.



1 2 3-5

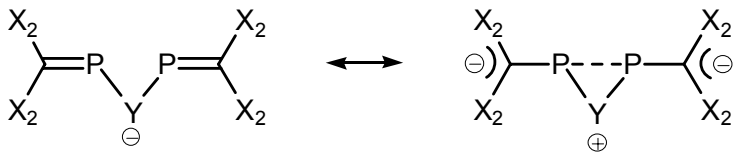
1,2 X_1= H, NH_2; **3** Y= P; **4** Y= As; **5** Y= Sb; X_2= H, CH_3, CF_3, SiH_3, $SiMe_3$

1 is a phosphenium cation stabilized by two electron-donating phosphaalkene groups. Surprisingly, no joint π-system has been found for **1** but the separated positively charged amidinium cationic groups and negatively charged PPP moiety, and the amidinium moieties are rotated out of the PPP plane. The calculated charge distribution agrees well with the geometry parameters evaluated for the corresponding equilibrium structures. The P-C distances correspond rather to the single bond whereas the P-P distances are close to the double bonds. These indicate mesomeric forms **B** and **C** strongly contributing into the final charge distribution.



A B C

In contrast, in anions **3-5** negative charge is delocalized at the terminal groups. The PYP angles are less than 90 degrees and decrease in series Y= P, As, Sb. The distances between the phoaphaalkene phosphorus atoms are significantly shortened forming the PYP cyclic system as a result of homoaromaticity of the moiety. The contribution of the mesomeric form **D** strongly increases for the electron withdrawing substituents X_2.



3-5 **D**

The calculated structure parameters of models **3,4** agree well with the experimentally investigated structures of the real compounds.

Water-assisted mechanism of 2-aminooxazole formation in prebiotically plausible conditions – *ab initio* study

Rafał Szabla and Robert W. Góra

[1]Theoretical Chemistry Group, Institute of Physical and Theoretical Chemistry, Wrocław University of Technology, Wybrzeze Wyspianskiego 27, 50-370 Wrocław, Poland

The question of the origins of life on Earth is perhaps one of the most fundamental and ancient, however, only recently the development of chemistry and biology allowed the scientists to examine the possible ways of formation of biological compounds from simple inorganic substrates. It is well established that one of the most important roles on early Earth was played by a polymer, which served to hold information and provided catalytic activities. In order to the 'RNA world' theory, the informational polymer was RNA. The confirmation to the hypothesis are 'molecular fossils' – essential sequences of RNA that play key roles in many processes in modern organisms. Nevertheless, the assumption that RNA chain components (ribonucleotides) must have formed from a ribose sugar, a nucleobase and phosphate have encountered many difficulties. It has been proven that the synthesis of purine nucleosides from sugar and nucleobase is inefficient. Not until 2009 was the first RNA nucleotide synthesized in prebiotically plausible conditions by Powner *et al.* [1]. The Authors proposed an entirely different pathway for pyrimidine ribonucleotide synthesis, in which the sugar and nucleobase emerge from a common precursor *i.e.* 2-aminooxazole (Fig. 1).

The purpose of the study was to find the accurate mechanism of 2-aminooxazole formation in prebiotically plausible conditions with using computational chemistry methods. The investigated reaction consists of 4 steps and it has been treated as a water-assisted reaction, where water acts as a bridge for proton transfer. The mechanism was determined both in gas phase and in solution. The study is also a comparison of different ab initio methods – MP2 and two DFT hybrid functionals (M06-2x and B3LYP).

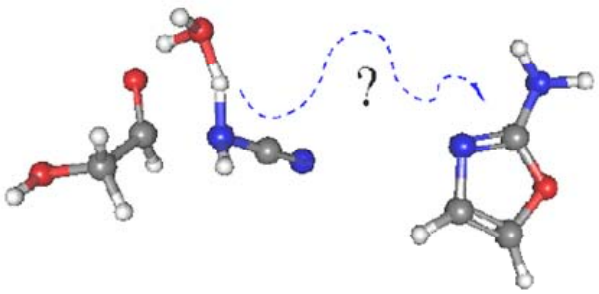


Fig. 1: Schematic drawing showing a preliminary transition state of the inorganic substrates: cyanamide, glycolaldehyde and water molecule and final product *i.e.* 2-aminioxazole

[1] Powner, M. W.; Gerland, B.; Sutherland, J. D. *Nature* **2009**, *459*, 239–242.

Acknowledgements: Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

Classification of binding site conformations on the example of protein tyrosine phosphatase 1B (PTP1B)

Vsevolod Yu. Tanchuk, Volodymyr O. Tanin, Andriy I. Vovk

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, Murmanska, 1, 02660, Kyiv-94, Ukraine; e-mail: v_tanchuk@yahoo.com

PTP1B is one of the most promising therapeutic targets for potential treatment of type 2 diabetes and obesity. That is why the enzyme is widely represented in the RSCB Protein Data Bank. We have found 91 PDB files which include 102 chains of PTP1B. We think that in cases like PTP1B, where a substantial amount of crystallographic data exists, it is possible and necessary to use ensemble docking. On the other hand, it is not desirable to dock to all conformations of the enzyme. All existing active centre conformations should be clustered by their similarity and cluster centroids used as an ensemble of structures.

The available conformations have been analyzed and clustered by a specially designed software tool. The ACTPDBCMP (Active Part of PDB Comparison) looks for a specified group of residues in specified PDB files, performs pairwise comparison of the found fragments to build a distance matrix, and finally performs hierarchical cluster analysis. Besides that mobility of each residue is determined. We have chosen 32 residues in both catalytic and vicinal binding sites of PTP1B and the residues of the WPD loop which plays an important role in the enzyme's catalytic mechanism. The results of clustering are summarized in the following table:

Cluster	Centroid (PDB code)	Number of structures	RMSD from ligand-free 2NHP (Å)	WPD-loop	Comments
1	2HNP	1	0	Open	Ligand-free
2	1OEM	2	2.84	Open	Oxidized
3	1NL9	7	1.37	Open	
4	1PHO	15	1.02	Open	
5	2CNF	22	2.39	Closed	
6	1Q6M	11	2.51	Closed	
7	2CM8	44	2.23	Closed	

It is interesting to note that ligand-free and oxidized forms of the enzyme are represented by separate clusters which are substantially different from the other cases. This emphasizes the importance of induced fit and makes construction of binding conformations from the structure of a free enzyme, as has been suggested earlier, somewhat problematic. Examination of the centroids shows that they differ significantly in the conformation of the residues of the WPD loop as well as conformations of Arg47, Arg24 and Lys120. The obtained clusters can be used for design of compounds that may be applicable as potent and selective inhibitors of PTP1B. The difference between clusters is sometimes striking:

Experiment, pKi	2CM8 (cluster 7)	1Q6M(cluster 6)	1PHO(cluster 4)	1NL9(cluster 3)
7.37	7.31	12.41	4.59	5.05

(experiment - compound 3, Cheuk K. Lau et. al., Bioorganic & Medicinal Chemistry Letters 14 (2004) 1043–1048, other results - docking by QXP/FLO+)

It means that all types of binding (represented by clusters) should be tested.

Bioactive nanoscale supramolecular assemblies of ionic and non ionic oligoperoxide based surfactants with drugs, DNA and RNA in water

O. Zaichenko[a], N. Mitina[a], T. Skorokhoda[a], E. Filyak[b], N. Boiko[b], L. Ivanytska[b], A. Riabtseva[a], M. Moskvin[a], V. Novikov[a], R. Stoika[b]

[a]Lviv Polytechnic National University, 12 S. Bandera St., 79013, Lviv, Ukraine; E-mail: zaichenk@polynet.lviv.ua

[b]Lviv Institute of Cell Biology, 14/16 M. Dragomanov St., 79005, Lviv, Ukraine

Novel heterofunctional carbon chain oligoperoxides were used as multi-site radical initiators for controlled synthesis of surface-active comb-like and block copolymers combining links and branches of cationic, anionic or/and nonionic polyethylene glycol (PEG) type. The surfactants were of controlled functionality, chain length, solubility, surface activity and reactivity. There was shown the formation of non stoichiometric intermolecular complexes via mechanisms of electrostatic interaction, due to formation of hydrogen bonds as well as a result of hydrophobic interaction providing arising nanoscale supramolecular structures in the media of various polarities. The formation of highly stable nanoscale supramolecular assemblies of oligomers and polymers of ionic and non ionic natures with low molecular weight and polymeric substances such as anionic or cationic surfactants including polyelectrolytes, antimicrobial and anticancer drugs, plasmid DNA and RNA were studied using conductometry, turbidimetry, dynamic light scattering, NMR, IR-, UV- spectroscopy and other chemical and physical-chemical techniques. The intermolecular complex formation accompanied by sharp change of physical-chemical properties of the mixtures in narrow component concentration range was observed. This witnesses the arising highly dispersed new phase comprising of micelle-like hydrophobic zones as a result of oligoperoxide surfactant and other component interaction stabilized by surfactant hydrophilic fragments. The main driving forces of the phenomenon are electrostatic and hydrophobic interactions. The formation of nanoscale hydrophobic zones in the system was confirmed by both light scattering technique and water insoluble drug solubilization. It was established that such water preparations provide essential enhancement of antimicrobial and anticancer activity due to synergism of simultaneous action of medicines and oligoperoxide based carriers.

State-to-state quantum reactive dynamics

Dmytro Babyuk

Chernivtsi National University, Ukraine

Detailed dynamical information for elementary act of chemical reaction requires knowledge at complete state-to-state level. It implies solving the time-independent Schroedinger equation for reactive scattering problem. The ultimate goal of such an approach is obtaining the complete *S*-matrix as a function of the collision energy. Its squared elements provide the transition probabilities from a definite initial state into a final state and are called state-to-state probabilities. Since this approach scales as N^3, where N – is basis set dimension, more attractive is a wave packet method which scales as N^2. Its basic idea is to solve the time dependent Schroedinger equation and then transform the time-dependent wave function into a time-independent one using the Fourier transformation. A single wave packet propagation gives only one column of the *S*-matrix for a wide range of the collision energy.

The aim of this research is to study the state-to-state dynamics of the exchange reaction H' + HCl → H'Cl + H. In general, this system has six degrees of freedom. But our study is limited to a case of zero total angular momentum ($\vec{J}$=0) and the total number of degrees of freedom is reduced to three.

The potential energy surface for this system called BW2 was derived in [1]. It was computed using internally contracted multireference configuration interaction (MRCI) wave functions with complete active space self-consistent field (CASSCF) reference wave functions. The Davidson correction (+*Q*) was applied to the final energies. The atomic orbital (AO) basis set for chlorine was derived from the augmented correlation consistent quintuple zeta basis set aug-cc-pV5Z,[8s7p5d4f3g]; for hydrogen, the aug-cc-pVQZ[5s4p3d2f] was used. In total, this basis set contains 289 primitive AOs, contracted to 201 functions. The scaled external correlation (SEC) correction was applied in order to compensate the barrier height lowering.

The dynamical study was performed using the Jacobi coordinates for reactants. The initial condition was a product of the Gaussian wave packet along the translational coordinate and rovibrational eigenstate $v_0 j_0$ along the remaining coordinates. The time-dependent wave function was expanded into a body fixed angular basis set. Its dependence on linear coordinates was treated by the grid method. The split-operator method was used as a time propagator. The propagated wave function was mapped at particular points into the product Jacobi coordinates in order to extract the state-to-state probabilities.

The calculations were carried out for the $v_0 = 0$, $j_0 = 0,1$ initial rovabritional states and the collision energy up to 2.85 eV. Some state-to-state probabilities are very sensitive to the change of collision energy. In some ranges of energy many probabilities reveal the oscillatory structure. These oscillations are not artifacts because changing the parameters of numerical integration does not effect the oscillatory structure. Most likely the oscillations are caused by the dynamical resonance phenomenon. The cumulative probabilities of final state have no oscillations. It can be explained that the oscillations of the state-to-state probabilities cancel each other and their summation gives smooth cumulative probability. Detailed analysis shows that the probability oscillations of final rotational states with the same parity have the coincident phase. If the parities are different, the phases are opposite. Such correlation leads to smoothing the cumulative probability.

Even at the lowest collision energy after the reaction threshold, final excited rotational states are more populated than the ground state. In general, the collision energy grows, the higher excited rotational states get populated. But for some states the gaps happen. It can also be caused by dynamical resonance. At high collision energy even the state j_f=18 is slightly populated.

[1] Bian W, Werner H.-J., *J.Chem.Phys.* **112** (2000) 220-229.

Structure, IR and UV-vis spectra of the triphenylamine-rhodanine dye studied by DFT

G. Baryshnikov, B. Minaev, V. Minaeva, A. Pidgorna

Bohdan Khmelnitsky National University, 81, Shevchenko blvd., Cherkassy, Ukraine, 18031; e-mail: glebchem@rambler.ru

The optimization of the triphenylamine-rhodanine dye molecule (TPAR) was performed based on the density functional theory (DFT) in the 6-31+G(d) basis set using the B3LYP hybrid exchange-correlation functional. This method is based on the combination of the Becke's three-parameter exchange functional (B3) and the Lee-Yang-Parr correlation functional (LYP). Using the same method, we calculated the frequencies and intensities of the IR absorption bands of TPAR molecules. The electronic absorption spectra were calculated according to the time-dependent density functional theory (TDDFT). To simulate the effect of a solvent on the electronic absorption spectra, we calculated the electronic excitations using the polarized continuum model (PCM). As a model solvent, we chose acetonitrile (CH_3CN), since it one of the most frequently used electrolytes in DSSC prototypes. Comparing the results obtained by the TDDFT/B3LYP method with experimental data, we noticed that they are considerably different. For this reason, we calculated excitations by other exchange-correlation functionals, namely, B3PW91 (Becke exchange functional (B3) and Perdew-Wang 1991 correlation functional (PW91)), mPW1PW91 (Perdew-Wang 1991 exchange functional as modified by Adamo and Barone (mPW1) and Perdew-Wang 1991 correlation functional (PW91), and PBE1PBE (Perdew-Burke-Ernzerhof exchange-correlation functional). We have found that the B3 exchange functional yields a large error in calculating the TPAR excited states compared both to experiment and to the mPW1 and PBE1 exchange functionals. The LYP, PW91, and PBE correlation functionals are equally good for calculating the TPAR excited states. Despite different energies and intensities of electronic transitions yielded by different functionals, all of the functionals show the same nature of these electronic transitions.

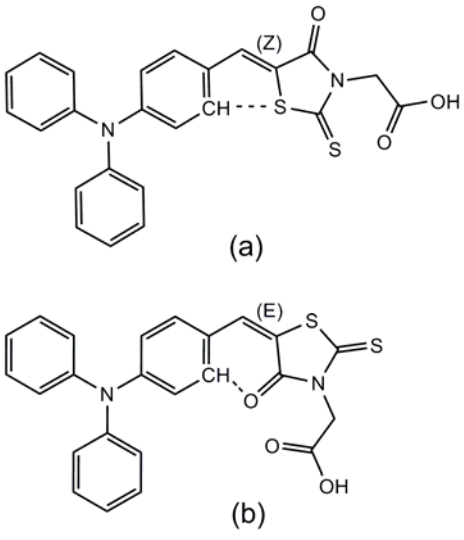


Fig. 1. Structure of Z (a) and E (b) isomers of TPAR molecules.

The quantum-chemical modeling of the structure and spectral properties of the TPAR molecule allow us to draw the following conclusions.

(1) The dye molecules exist mainly in the form of the Z isomer (Fig. 1), which is caused by sulfhydride interactions and by the advantageous relative spatial positions of substituents with respect to the double band.

(2) The absorption of the dye in the visible region is caused by one single-electron singlet-singlet excitation with charge transfer from the triphenylamine donor group to the rhodanine acceptor group [1].

(3) The calculated IR spectrum of the dye coincides with the experimental data in all details, which allows one to unambiguously assign all the absorption bands observed in the IR region based on the analysis of normal vibrational modes.

[1] Baryshnikov G., Minaev B., Minaeva V. // Opt. Spectrosc. – 2011. – Vol. 110, N 2. – P. 216-223.

Superposition-additive approach. Calculation of thermodynamic aspects of clusterisation of substituted alkanes at the air/water interface

Yu.B. Vysotsky[a], E.A. Belyaeva[a], E.S. Fomina[a], R. Miller[b]

[a]*Donetsk National Technical University, 58 Artema Str., 83000 Donetsk, Ukraine; e-mail: eabelyaeva@mail.ru*

[b]*Max Planck Institute of Colloids and Interfaces, D-14424 Potsdam/Golm, Germany*

The superposition-additive approach is based on the presumption that atoms exist in molecules in such a way that the 'individuality" of each atom (or atomic group) remains the same in various chemical combinations, i.e. in different molecules. This property is referred to as the transferability of the atomic properties in a molecule. Also, the atomic values, being summed over all the atoms in the molecule, yield the molecular average; therefore the corresponding molecular characteristics are additive. The superposition-additive approach is based on the transferability of atomic properties and the additivity of molecular properties; the essence of the procedure is the assumption that when two molecular graphs are virtually superimposed, the properties of the constituent atoms remain unchanged. If the same superposition can be constructed in two different ways, each one involving two entities (ions, radicals, clusters etc.), it becomes possible to calculate the structure and properties of one of these entities, the structure and properties of the remaining three entities being known.

The applicability of this approach for the calculation of the thermodynamic parameters of clusterisation at the water/air interface of fatty alcohols, thioalcohols, amines, nitriles, fatty carbon acids ($C_nH_{2n+1}X$, X is the functional group) and *cis*-monoienic carbon acids ($C_nH_{2n-1}COOH$) is studied. It is shown that to apply the superposition-additive approach for the description of the thermodynamic parameters of clusters, the superposition-additive schemes should be used which ensure the correct account for the intermolecular CH···HC interactions. This requirement imposes certain restrictions on the superimposed structures as compared with the structures used in the additive method: in the superposition-additive method the correct configuration should ensure the matching of the molecular graphs and the relevant intermolecular CH-CH interactions. In particular, for the description of the clusters of substituted alkanes with even or odd number of carbon atoms in the hydrocarbon chain, the structures should be used with the same parity of the carbon atoms number in the superimposed constituents. The thermodynamic parameters were determined using the proposed approach agree well with the available data, calculated using the quantum chemical semiempirical method PM3 (Direct Calculation).

Table 1. Enthalpies of clusterisation of thioalcohols calculated via superposition-additive approach (SAA)

System	Dimer		Trimer		Tetramer	
	SAA	Direct Calc.	SAA	Direct Calc.	SAA	Direct Calc.
ΔH_m/m, kJ/mol						
$C_{10}H_{21}SH$	−248.64	−248.69	−257.31	−257.60	−261.70	−260.64
$C_{11}H_{23}SH$	−272.54	−272.55	−281.48	−281.60	−285.93	−285.96
$C_{12}H_{25}SH$	−299.14	−299.21	−309.79	−309.84	−312.55	−314.83
$C_{13}H_{27}SH$	−323.09	−323.10	−333.81	−333.85	−339.10	−339.14
$C_{14}H_{29}SH$	−349.72	−349.75	−362.08	−362.01	−369.02	−367.97
$C_{15}H_{31}SH$	−373.65	−373.66	−386.09	−386.11		
$C_{16}H_{33}SH$	−400.29	−400.30	−414.18	−414.25		

The possible mechanims of action of calix[4]arene C-99 with ligand-bindings center of subfragment-1 ATPase of myometrium

O. V. Bevza, A. A. Bevza, S. O. Kosterin

Palladin Institute of Biochemistry, National Academy of Sciences of Ukraine, Kyiv; e-mail: sbevza@biochem.kiev.ua;

With applying the modern methods of computer design, in particular GRID-technology, it was planned to get new data which will be important for understanding of biochemical and biophysical conformities to law of the phenomenon of electro- and pharmacomechanics coupling in smooth muscles; thus, the question is about realization of computer design of interaction of retractive and transport proteins with biologically-active ligands (ATP, calix[4]arenes). On the basis of the got models to carry out a molecular design and synthesis biologically of active substances.

With the help of computer design the interaction of calixa[4]rene C-99 with myosin subfragment-1 of myometrium has been investigated. Several mechanisms involved in the calixa[4]rene C-99 inhibition of myosin head ATPase were supposed and participation of hydrogen, hydrophobic and electrostatic interactions in these mechanisms was discussed.

In the search for a possible mechanism of interacting between calix[4]arene C-99 (as ligands) with the functionally active part of the myosin subfragment-1 molecule (as receptor), a three-dimensional structure of calix[4]arenas in the complex was modelled. For this purpose we used the spatial structure of myosin, ID 1B7T in the Protein Data Bank.

In modeling experiments, Mg^{2+} and (or) molecule ATP (ADP) were placed in the enzyme active center as they are naturally necessary for the work of ATPase. A search for the most powerful and advantageous mutual docking location of ligand (C-99) was conducted in the spacious molecule of myosin. It has been shown that calix[4]arene C-99 inhibited of myosin subfragment-1 ATPase of myometrium. This inhibition is noncompetitive to ATP and Mg^{2+}. At the same time, this compound reduces the enzymatic hydrolysis apparent maximum rate of nucleoside triphosphate with respect to ATP and Mg^{2+}.

It has been analysed of different types of interacts, which characterize the complexes of ligands with the ligand-binding areas of subfragment-1 ATPase of myometrium. Identified amino-acid sequences, which interact with this ligands, the type of their interacting with receptors is research. Possible assumption that the calixarenes interacted with the functionally active part of the myosin molecule (the area near ATP-binding center) was supported by the result of docking. Predicted in silico binding of calixarenes in this area was confirmed by the results of calixarenes influence on the catalytic activity of myosin (subfragment-1) in vitro.

There were certain areas in a ligand-bindings center to the subfragment - 1 miosin, at being of Mg^{2+} as of the cofactor, which can be responsible for interaction of ligands with a receptor, and to pick up conditions for realization of GRID-investigates.

By the method of molecular dynamics by means of the program GROMACS (what uses plenty of parameters of simulation), there was the conducted calculation of dependence of conformation descriptions of complexes ligand-receptor from time, which confirmed results which were got by the method of docking.

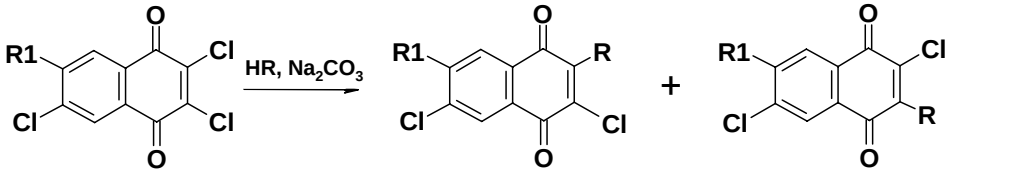
The data presented here demonstrate that the calixarenes which have been studied can influence uterus smooth muscle function at the level of the contractile proteins, namely ATPase.

Investigation of reaction mechanism and isomerism by quantum-chemical calculations of program HyperChem 8

Buchkevych I.R., Figurka O.M., Stasevych M.V., Musyanovych R.Ya., Novikov V.P.

National University "Lviv Polytechnic", Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, 12 S. Bandera Str., Lviv, 79013, Ukraine; e-mail: vnovikov@polynet.lviv.ua, vladnovikov@list.ru, vladnovikov@ukr.net

Interaction of 7-nitro- **1** and 7-amino-2,3,6-trichloro-1,4-naphthoquinone **2** with the appropriate amine or amino acid was carried out nucleophilic substitution of chlorine atom on the amino group in quinonic cycle with the formation of regioisomer pairs **3**, **3 '(a-e)** and **4**, **4 '(a-d)** in different proportions depending on the substituent R_1.



1, 2 3, 4 (a-e) 3', 4'(a-e)

R1 = NO_2 (1), NH_2 (2)

R= —N O (a); —N (b); —N —COOH (c); -N-(*n*-Bu)$_2$(d); —$NH(CH_2)_3COOH$(e);

Determined that at presence nitrogroup in position 7 of naphthoquinone substitution passes on both chlorine atoms to form regioisomer pairs **3 (a-e)**, **3 '(a-e)** about a 1:1 ratio, and the presence of amino group in the position 7 **4 (a-d)**, **4 '(a-e)** - regioisomers ratio 6:1.

Quantum-chemical calculations were carried out by *HyperChem 8*, charges on atoms, energies, HOMO and LUMO, space structure were calculated which demonstrate the existence of isomerism and determine the of mechanism reaction.

The results of quantum-chemical calculations using *HyperChem 8* and the calculation of the space structure of molecules of 7-amino(nitro)-3(2),6-dichloro-2(3)morpholino-1,4-naphthoquinones showed that the charge on the carbon atom located in position 2 is lower than on carbon atom in the position 3 what is also confirmed by the formation of different regioisomer ratios.

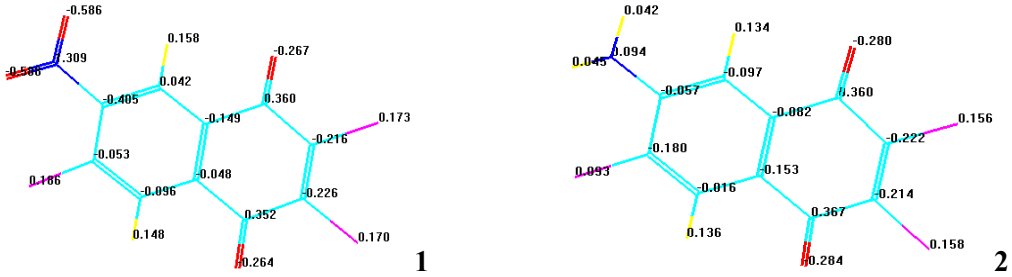
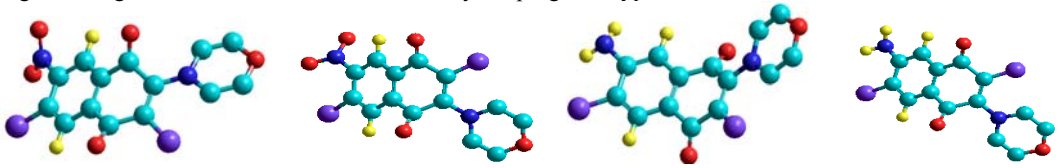


Fig. 1. Charges on atoms of molecules **1** and **2** by the program HyperChem 8



-94580.72 (J/mol) **3a** -96759.79 (J/mol) **3'a** -81825.49(J/mol) **4a** -89903.00(J/mol) **4'a**

Fig. 2. Space structure and formation energy of molecules **3a**, **3'a** and **4a**, **4'a** by HyperChem 8.

Complete basis sets (CBS) estimation of harmonic and anharmonic frequence of water, formaldehyde, formamide and *N*-methylformamide in solution

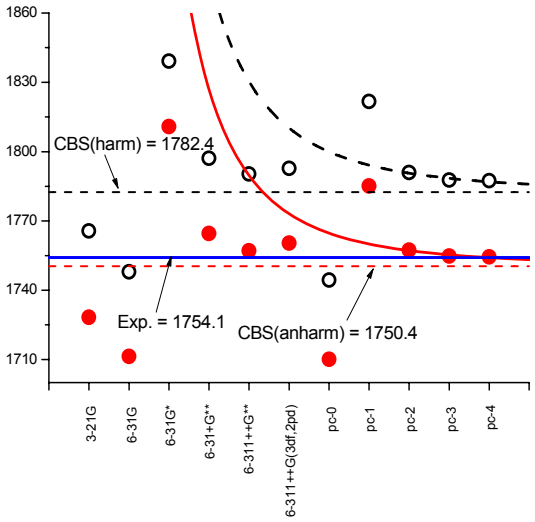
Aneta Buczek, Teobald Kupka, Małgorzata A. Broda

Faculty of Chemistry, University of Opole, 48, Oleska Street, 45-052 Opole, Poland

Harmonic and anharmonic frequencies of fundamental vibrations of the title compounds in the gas phase and in several solvents were successfully estimated in the B3LYP Kohn-Sham limit. The obtained results with correlation-consistent and polarization-consistent basis sets were fitted with two-parameter formula. Anharmonic corrections using the second order perturbation treatment (PT2) and hybrid B3LYP functional combined with polarization consistent pc-n (n=0,1,2,3,4) and several Pople's basis sets were analysed for all fundamental vibrational modes in the gas phase and solution. Solvent effects were modelled within a PCM method.

The anharmonic frequency of diagnostic amide vibration C=O in the gas phase and in chloroform solution, calculated with the VPT2 method was significantly closer to experimental data than the corresponding harmonic frequency. Both harmonic and anharmonic frequencies of C=O stretching mode decreased linearly with solvent polarity, expressed by the relative permittivity ratio $(\varepsilon-1)/(2\varepsilon+1)$.

An example of convergence toward the CBS limit of C=O harmonic and anharmonic frequencies of formamide in the gas phase is shown below. The CBS values in solutions are similar and the estimated value depend on the polarity of the solvent.



The increase of Pople and Jensen basis set quality does not warrant improved agreement of all anharmonic frequencies with experimental values and some low frequency modes significantly overestimate the experiment (by about 2250 cm^{-1} in case of NH_2 in plane bending calculated at B3LYP/6-31G* level of theory).

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[3] A. Buczek, T. Kupka, M. A. Broda J.Mol.Model., (2010), DOI: 10.1007/s00894-010-0944-9

Acknowledgments Aneta.Buczek is a recipient of a PhD fellowship from a project funded by the European Social Fund. Calculations were carried out in Wroclaw and CYFRONET,AGH,Kraków,grant MEiN/SGI3700/UOpolski/063/ 2006.One of us(T.K.) was supported by grant 10/WCH/2010-S.

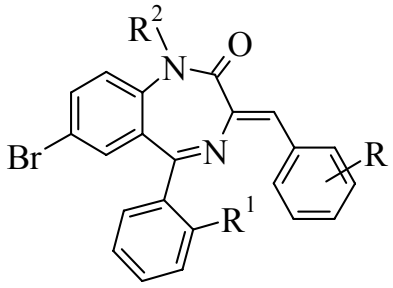
Synthesis, affinity and QSAR-analysis of new potential ligands of benzdiazepine CNS receptors of 3-arylidene-1,2-dihydro-3*H*-1,4-benzodiazepine-2-ones

V.I. Pavlovsky, N.A. Burenkova, S.Yu. Bachinsky, I.A. Boyko, S.A. Andronati, A.G. Artemenko, V.E. Kuz'min

A.V. Bogatsky Physico-Chemical Institute of the NAS of Ukraine, 86 Lustdorfskaya doroga,Odessa 65080, Ukraine; e-mail: medchem_department@ukr.net

In order to search for potential selective ligands of the central (CBR) and peripheral benzdiazepine receptors (PBR) CNS a series of new 3-arylidene-1,2-dihydro-3*H*-1,4-benzodiazepine-2-ones (**1-8**) were synthesized by us by methods described previously [1].

According to the analysis of structure - affinity - selectivity of binding to the benzdiazepine receptors statistical models were designed, molecular design and computer screening of new selective derivatives of 1,4-benzodiazepine-2-one were conducted on the basis of QSAR-analysis data published earlier in [2], and target compound **9-11** were synthesized similarly [3].



R^1=R^2=H: R=2-Cl (**1**), R=3-Cl (**2**), R=4-Cl (**3**);

R^1=Cl, R^2=H: R=2-Cl (**4**), R=3-Cl (**5**), R=4-Cl (**6**), R=3,4-Cl_2 (**7**), R=2,6-Cl_2 (**8**);

R^1=Cl, R^2=CH_2COOCH_3: R=2-Cl (**9**), R=3-Cl (**10**), R=4-Cl (**11**).

The method of radioligand analysis examined the ability of the synthesized compounds **1-11** to displace competitively the radioligands [^{3}H]PK11195 and [^{3}H]flumazenil from their places of specific binding to PBR and CBR, respectively.

Compounds **2**, **5** and **7** binding preferentially to CBR, compounds **4**, **8** and **10** exhibiting affinity for both receptor type were identified among the investigated substances. It was found that the target compounds **9** and **11** are PBR high-affinity ligands, and compound **9** selectively binds to PBR (Ki (CBR)> 10000 nM).

The values of affinity (K_i), calculated and obtained experimentally are K_i (predicted) 104.4 nM and K_i (exp.), 89.3 nM for compound **9**, K_i (predicted) 119.1 nM and Ki (exp.) 112.3 nM for compound **11**, respectively.

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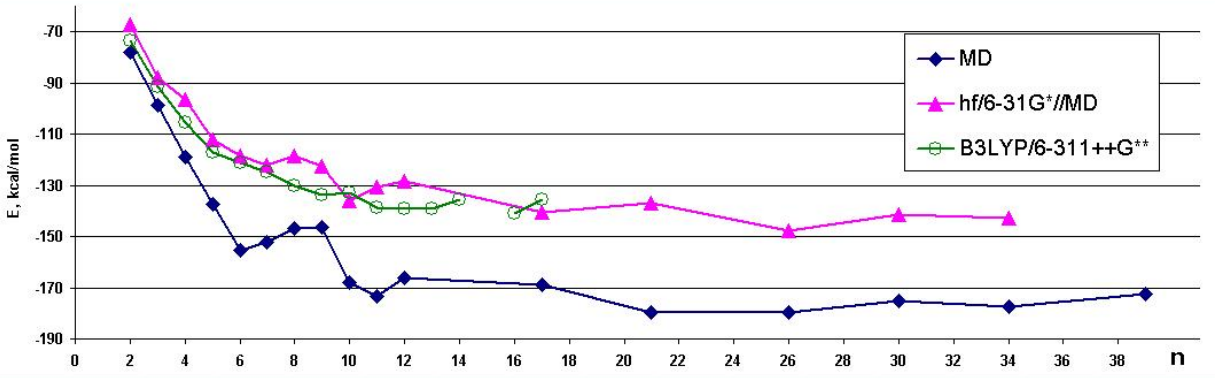
Analysis of Gas Phase Conformations of Poly(ethylene glycol) Oligomers Complexes with Na^+, K^+ and Cl^- ions

V.V. Chagovets, V.G. Zobnina, M.V. Kosevich

B. Verkin Institute for Low Temperature Physics and Engineering of the NAS of Ukraine, 47 Lenin Ave., Kharkov 61103, Ukraine; e-mail: vchagovets@ilt.kharkov.ua

Many existing and promising applications of polyethers, poly(ethylene glycol) (PEG) in particular, cause the necessity of deep investigations of their properties and intermolecular interactions. In basic experimental studies of PEG-ion interactions, stable complexes of PEG_n oligomers with both monoatomic cations $PEG_n•Na^+$, $PEG_n•K^+$ and anion $PEG_n•Cl^-$ have been observed in the gas phase under mass spectrometric conditions. Simulation of such complexes, however, meets with a difficulty connected with a large number of degrees of freedom of the polymers and low potential barriers between numerous minima at the potential energy surface resulting in high conformational mobility of the polymeric chain. This makes practically impossible selection of the most energetically favourable conformation by simple looking over all possible conformations. A helpful approach is a so called annealing procedure in the framework of molecular dynamics simulation, described in M. Bowers works [1]. In the present study this approach was applied to a set of gas phase complexes of PEG_n oligomers with polymerization degrees n = 2-12, 17, 21, 26, 30, 34, 39 with Na^+, K^+, and Cl^- ions. For the most stable complexes obtained by molecular dynamics with a CHARMM force field, *ab initio* HF/6-31G* quantum chemical calculations were performed.

The annealing procedure consisted in a cyclic 100-fold repetition of heating of a complex up to 800 K, retention at this temperature during 30 ps followed by a stepwise cooling down to 0 K with retention at each step for 1 ps for structure equilibration. The energy minimization for thus obtained geometries by means of molecular mechanics resulted in a set of 100 PEG-ion structures which corresponded to local minima at the potential energy surface. Among them the structure with the lowest energy was selected as the most stable. For these structures oligomer-ion interaction energies (E, kcal/mol) were calculated and plotted *vs* the polymerization degree n, as exemplified in the Figure below for $PEG_n•Na^+$ complexes.



The interaction energies for the complexes calculated by HF/6-31G* method appeared to be somewhat lower but followed the same no monotonous trend.

Comparison with the literature data [2] on interaction energies in $PEG_n•Na^+$ complexes obtained by B3LYP/6-311++G** with optimization have shown good agreement with our HF/6-31G* data, which allowed us to suggest more time-saving route of calculations consisting of optimal geometry determination by molecular dynamics with annealing followed by energy calculations by quantum chemical techniques.

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The comparison of the vibrational spectra of methanol gas and methanol in argon matrixes with the results of the simulation using the method of molecular dynamics

Chernolevskaya Ye.[a], Borzda T.[a], Doroshenko I.[a], Pogorelov V.[a], Isayev A.[b], Gorb L.[b], Sablinskas V.[c], Balevicius V.[c]

[a] *Kyiv National Taras Shevchenko University, Glushkova av., 4, build.1, Kiev, Ukraine*

[b] *Interdisciplinary Center for Nanotoxicity, Jackson MS, USA*

[c] *Vilnius University, Sauletekio, 9-3, Vilnius-10222, Lithuania*

In our work we present the comparison of the in experiment obtained spectra of methanol in argon **matrixes** at temperatures from 10 to 50 K with the results obtained from the computer simulation using the method of molecular dynamics (MD) and quantum chemistry.

It was found that the results of MD simulations using a box with size of 15 A correlate with the results of experimental data of methanol in argon **matrixes** at the appropriate temperature.

Also we have compared the IR absorption spectra of methanol gas with modeling spectra of methanol obtained from using the MD method. The results of our studies show that the five-molecule clusters of methanol fixed not only in the liquid, but also in the gas phase, and this result is according to the results of MD simulation.

Ab initio calculation of electronic structure of $Li(Na)_2B_4O_7$ crystals

I. Chobal[a], I. Rizak[b] and V. Rizak[a]

[a] *Uzhhorod National University, 88000 Uzhhorod, Ukraine*

[b] *National Aerospace University of "KhAI," 61000 Kharkov, Ukraine*

Lithium tetraborate ($Li_2B_4O_7$) possesses a combination of physical properties which are important for practical applications, and it finds wide are important for practical applications and fundamental research. For example, it is a promising material for piezotechnology, acoustoelectronics [1], and nonlinear optics [2].

In this work, the optimized configuration and electronic structure of the cluster models of lithium tetraborate and sodium tetraborate crystals, containing 1–8 formula units of the $Li(Na)_2B_4O_7$ compound, were calculated from first principles. All calculations were performed with the GAMESS (US) quantum-chemistry package [3] by using the resources of the cluster at the Glushkov Institute of Cybernetics of the National Academy of Sciences of Ukraine. The calculations have been performed using the spin-restricted Hartree-Fock method in the 6-31G split-valence basis set.

It has been shown that the clusters are stable and retain the topology of the simulated crystal. The characteristic maxima of the total density of states of different clusters are formed by identical atomic states, namely, the top of the valence band is primarily formed by O *p* states, whereas the low-temperature part of the spectrum is formed by the O *s* states. The calculated results are compared with available experimental data from the literature. The influence of the cluster sizes on the properties under investigation has been analyzed.

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[3] M. W. Schmidt *et al.*, J. Comput. Chem. **14**, 1347 (1993).

Effects of pressure on the electronic structure and vibrational properties of $Sn_2P_2S_6$ crystals: *ab initio* calculation

O. Chobal[a], I. Rizak[b], V. Sabadosh[a] and V. Rizak[a]

[a] *Uzhhorod National University, 88000 Uzhhorod, Ukraine*

[b] *National Aerospace University of "KhAI," 61000 Kharkov, Ukraine*

Our studies [1] have shown that in the $Sn_2P_2S_6$-like crystal diagram the tricritical point and the Lifshitz point are located close to each other, while with the chemical composition and external pressure variation the tricritical Lifshitz point is realized in the P-T-x-y-diagram of the $(Pb_ySn_{1-y})_2P_2(Se_xS_{1-x})_6$ crystals. From the applied viewpoint, these materials are of current interest as temperature sensors and pressure gauges and hold much promise for the use in holography and nonlinear optics in the infrared region.

In this work the electronic structure and phonon spectra of $Sn_2P_2S_6$ crystals at external pressure were calculated from first principles. We performed our calculations using the plane wave density functional theory (DFT), program ABINIT [2], within local density approximation (LDA). All calculation were performed by using the resources of the cluster at the V.M. Glushkov Institute of Cybernetics of the National Academy of Science of Ukraine. The Troullier-Martins normconserving pseudopotential was used with a plane wave kinetic energy cutoff of 30 Ha. Brillouin zone integration for charge density and total energy is performed with a 6x6x6 Monkhorst-Pack grid. We optimized the lattice geometry by the Broyden-Fletcher-Goldfarb-Shanno method and obtained values, which is only slightly different (<2%) from the experimental values at atmospheric pressure. Phonon spectra for $Sn_2P_2S_6$ crystals were calculated by using the density functional perturbation theory (DFPT).

The characteristic maxima of the total density of electronic states are formed atomic states, namely, the top of the valence band is primarily formed by S *p* states, whereas the low-temperature part of the spectrum is formed by the S and P s states. The phonon frequencies at the zone centre of Brillouin zone which are of interest for the interpretation of the infrared and Raman spectrum are presented. A symmetry analysis of the phonon modes at Γ point was performed, and calculated frequencies are compared to experimental spectra. The influence of the hydrostatic pressure on the properties under investigation has been analyzed.

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QSAR Analysis of Thiopirano[2,3-d]thiazoles as Potential Antitumor Agents

Iryna Drapak, Volodymyr Ogurtsov, Anna Kryshchyshyn, Roman Lesyk

Danylo Halytsky Lviv National Medical University; e-mail: chemdep@meduniv.lviv; iradrapak@ukr.net

Quantitative structure – activity relationship (QSAR) analysis is widely used nowadays as reliable method of biological activity prediction of different classes of organic compounds. Previous investigation of polycyclic thiopirano[2,3-*d*]thiazole derivatives activity allowed us to establish their high anticancer potential *in vitro*. Research area future progress has considerable potential for directed drug-like molecules design and synthesis.

QSAR analysis was performed to identify the electron-dimensional structural features of tested compounds responsible for the anticancer activity appearance. For the QSAR analysis 30 compounds (thiopirano[2,3-*d*]thiazole derivatives) were chosen and divided into two sets: isothiochromeno[4*a*,4-*d*]thiazole derivatives and chromeno[4',3':4,5]thiopyrano[2,3-*d*]thiazole derivatives.

Tested compounds structures optimization was carried out with the applying of HyperChem7.5 program using method of molecular mechanics (MM+) and semi-empirical quantum chemical method (AM1). The physicochemical properties of each compound were specified using various descriptors, which outline lipophilic, conformational, electronic, spatial, structural, thermodynamic and quantum-mechanical information.

Using testing compounds molecular structures basis and their known biological activity QSAR models were built with the applying of GA-MLRA method and BuildQSAR program, which allows generating of one- or multivariate models with the maximum value of correlation coefficient (r) and minimum value of standard deviation (s). Multivariate linear models have the form of equation: $activity = \sum x_i a_i + b_i$, were $\boldsymbol{x_i}$ denotes molecular descriptor. Tested compounds anticancer activity was expressed as mean percent of cancer cells growth (60 tumor cell lines representing all types of cancer: non-small cell lung cancer, colon cancer, breast cancer, ovarian cancer, leukemia, renal cancer, melanoma, prostate cancer) at single concentration of 10^{-5} M and was chosen as activity parameter. Quality of models was estimated using correlation coefficient (r^2), standard deviation (s), Fisher's coefficient (F); cross-validation was carried out using "lean-one-out" method and coefficient correlation evaluation.

Following models have the best statistical rates:

$$GI50\%(Leukemia/SR) = -121,9 - 8,23*R + 1,11*V$$
$$(n=9, {}^{r2}=0,972, S=0,91, F=50,4, q^2=0,885)$$
$$GI50\%(Prostate\ cancer/PC\text{-}3) = 403,1 - 1253,7*Ch{=}S + 0,00272*IAE + 2,814*R$$
$$(n=21, r^2=0,872, S=1,26, F=19,0, q^2=0,672)$$
$$GI50\%(Melanoma/SK\text{-}MEL\text{-}5) = 56,53 + 0,389*HF - 5,077*EH$$
$$(n=21, r^2=0,825, S=1,41, F=19, 0, q^2=0,549),$$

where R is the refractivity; V – molecule volume, Ch=S – charge of thiazolidine endocyclic sulfur atom, IAE – isolated atoms energy, HF – heat of formation, EH – hydration energy.

Obtained QSAR models are applicable for specific anticancer activity predicting of novel thiopirano[2,3-d]thiazole derivatives and may be a theoretical platform for the potential antitumor drug-like molecules *de novo* synthesis.

Excited state potential energy curves from a parameterized effective potential method

S.I. Fesenko, V.N. Glushkov and E.A. Siz'ko

Dept. of Physics, Electronics and Computer Systems, Dnepropetrovsk National University, Ukraine; e-mail: v_n_glushkov@yahoo.com

Nowadays, the optimized effective potential (OEP) based methods are considered to be as a promising technique for constructing local potentials of density functional theory in its orbital-dependent implementation. Different approximate analytical forms of the OEP were proposed to simplify an integral OEP equation. In particular, the exchange OEP methods for molecules based on Gaussian basis set appeared. However, the Gaussian basis set OEP methods for molecules suffer from numerical instabilities in the calculations. Therefore a number of approximations were introduced for constructing numerically stable OEP exchange potentials (e.g. [1] and references therein).

Unlike the Gaussian basis set OEP methods a parameterized effective potential (PEP) expressed in terms of the external potential has been proposed [2,3] and tested by *ground state* calculations. It was shown that the PEP method is free from numerical instabilities. In this communication the PEP method is extended to compute potential energy curves of *excited states* having the same symmetry. The PEP generates one-particle orbitals so that a Kohn-Sham determinant based on them is orthogonal to determinantal functions of low-lying states. A comparison of the PEP potential curves (*HeH* and H_2 molecules) with that obtained by time-consuming configuration interaction methods shows that the PEP method is capable of supporting a good accuracy for an equilibrium geometry and vertical excitation energies.

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Simple quantum chemical approach to calculation of 2D clusterization threshold temperature of amphiphilic compounds at the air/water interface

Yuri B. Vysotsky[a], Elena S. Fomina[a], and Reinhard Miller[b]

[a]*Donetsk National Technical University, 58 Artema Str., 83000 Donetsk, Ukraine*

[b]*Max Planck Institute of Colloids and Interfaces, D-14424 Potsdam/Golm, Germany*

The simple approach of calculation of 2D spontaneous clusterization threshold temperature of substituted alkanes at the air/water interface versus alkyl chain length was proposed using quantum chemical semiempirical method PM3. This approach was approved by way of example of eight classes of surfactants: amines, alcohols, thioalcohols, saturated and unsaturated carbon acids, α-amino acids and amides of carbon acids.

Table. The values of the coefficients for calculation of the thermodynamic parameters of clusterization per one monomer molecule of the infinite 2D cluster of substituted alkanes at 298 K

Surfactant	$\Delta H^{Cl}_{298,\infty}$, kJ/mol		$\Delta S^{Cl}_{298,\infty}$, J/(mol·K)	
	a	b	c	d
Alcohols	–3,49	–9,20	–144,8	–18,4
Amines	–4,96	–10,11	–166,0	–24,5
Thioalcohols	–7,40	–9,78	–211,9	–17,8
Fatty carbon acids	0,07	–10,39	–160,0	–23,1
Unsaturated carbon acids: *cis*- *trans*-	–47,42 –21,54	–9,20 –9,20	–341,7 –261,4	–18,4 –18,4
Amides of fatty carbon acids	–4,23	–10,24	–175,8	–22,3
α-Amino acids	–17,98	–10,28	–217,1	–21,7

The approach is based on the fact that, elongation of the alkyl chain of amphiphilic molecules causes the increase of intermolecular interaction energy between them that stimulates their close packing and structuring. It is simple to calculate Gibbs' energy of cluster formation per one monomer molecule (m) of infinite 2D clusters using the previously obtained regression expressions for determination of the enthalpy $\Delta H^{Cl}{}_{(T),\infty}/m = a + b \cdot K_a$, $\Delta S^{Cl}{}_{(T),\infty}/m = c + d \cdot K_a$ and the entropy of cluster formation calculated under condition of 298 K in the frameworks of PM3 method. Here K_a is the number of CH···HC-interactions per one monomer molecule of regarded films, corresponding coefficients a, b, c and d are listed in the Table. While having set Gibbs' energy equal to zero it is possible to obtain the formula for estimation of the temperature of the spontaneous clusterization threshold of considered classes of substituted alkanes: $T = (a + b \cdot K_a)/(c + d \cdot K_a)$. The relative error of estimation of the temperature of the spontaneous clusterization threshold on the alkyl chain length of the surfactants varies in range of 3-8%.

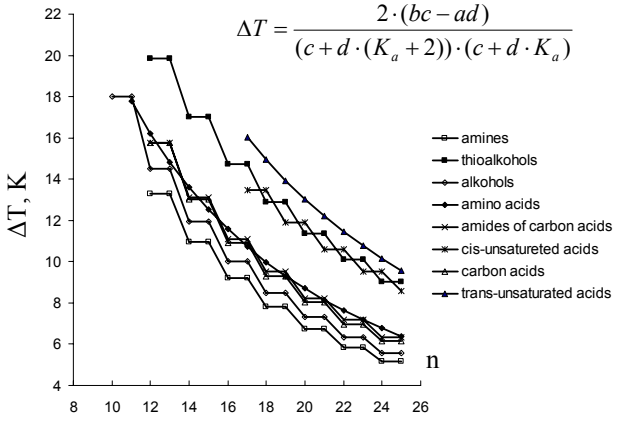


Figure. Dependence of the variation of the ΔT on the alkyl chain length

It should be mentioned that effect of the alkyl chain elongation of substituted alkanes on two methylene units is equal to subphase temperature reducing (ΔT) by 10-20 K that well agrees with present experimental data. Meanwhile, the difference between ΔT values for considered classes of amphiphilic compounds becomes less significant with the lengthening of the hydrocarbon chain of molecules (see Figure). This indicates basic contribution of intermolecular CH···HC-interactions between the alkyl chains in the 2D clusterization process.

Thermodynamic aspects of 2D cluster formation of aliphatic amides at the air/water interface in the PM3 approximation

Yuri B. Vysotsky[a], Elena S. Fomina[a], and Reinhard Miller[b]

[a]*Donetsk National Technical University, 58 Artema Str., 83000 Donetsk, Ukraine*

[b]*Max Planck Institute of Colloids and Interfaces, D-14424 Potsdam/Golm, Germany*

Nowadays polypeptide and proteins, that contain amide functional group, are widely studied because of development of the technologies that enable to construct different artificial biological membranes and sensors on the base of these compounds. In connection with mentioned facts the aim of this work was research of the thermodynamics of 2D cluster formation of aliphatic amides $C_nH_{2n+1}CONH_2$ (n=6-16) at the air/water interface at the temperature 293 K.

Conformational analysis of monomers shows the existence of two stable conformers with the next values of the dihedral angles ∠α=C2–C1–N–H1 and ∠β=C3–C2–C1–N (cf. Fig. 1): 165° and 78°, 165° and -84° for monomer 1 and monomer 2 respectively. Formation of these monomers is practically isoenergetic. Meanwhile, the regression dependencies of the thermodynamic parameters of amide formation on the alkyl chain length are linear, and the contributions of the methylene groups in the values of corresponding thermodynamic parameters coincide with ones obtained for previously considered classes of surfactants.

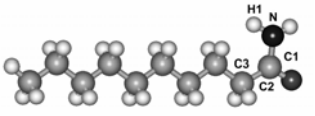


Fig.1. Dihedral angles of amide functional group

Dimers were constructed on the base of found monomers. They were conventionally divided on two types with 'parallel' and 'sequential' orientation of functional groups. It should be noted that the tilt angle of molecular chain axis with respect to the normal to the q-direction of the unit cell of 2D film in the 'sequential' dimers is φ=20,51˚, while for 'parallel' dimers the tilt angle of molecular chain axis with respect to the normal to the p-direction is δ=10˚. These values of angles φ and δ determine general tilt angle of the molecular chains of aliphatic amides with respect to the normal to the interface t=23˚ that agree with the GIXD data.

For small clusters (dimers, trimers and tetramers) of fatty amides the thermodynamic parameters of their formation and clusterization were calculated. On the base of obtained data the additive scheme was developed. It represents the enthalpy, entropy and Gibbs' energy values of clusterization of amides as the summarized contributions of the interactions between hydrophilic parts of molecules and intermolecular CH···HC interactions. It enables to calculate the values of regarded parameters for clusters of any dimension up to 2D films. The contribution of the intermolecular CH···HC interactions in to the values of the enthalpy and entropy of clusterization per one amide molecule was found to be -10,24 kJ/mol and -22,27 J/(mol·K) respectively, while the contribution of the interactions between hydrophilic 'heads' of molecules in regarded parameters were calculated to be -4.36 kJ/mol and -176.24 J/(mol·K) correspondingly. The dependencies of the enthalpy and entropy of clusterization per one amide molecule (m) on the alkyl chain length (n) are stepwise and can be expressed as follows:

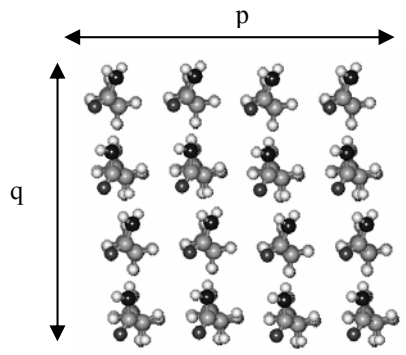


Fig.2. The fragment of infinite aliphatic amide 2D film

$$\Delta H^{Cl}_{293,\infty}/m = -20.48\cdot\left\{\frac{n}{2}\right\} - 4.36\,,\quad \Delta S^{Cl}_{293,\infty}/m = -24.54\cdot\left\{\frac{n}{2}\right\} - 176.24\,.$$

Here the braces {…} denote the integer part of the number. The threshold of the spontaneous clusterization of aliphatic amides is 14 carbon atoms at the temperature 293 K that agree well with experimental data.

Constrained optimized potential method vs time dependent DFT for excited states: small systems

T. Very [a], X. Assfeld [a], V. Glushkov [b]

[a] *Faculte des Sciences et Techniques, Nancy-Universite, Vandoeuvre-les-Nancy, 54506, France; e-mail: Xavier.Assfeld@cbt.uhp-nancy.fr*

[b] *Dept. of Physics, Electronics and Computer Systems, Dnepropetrovsk National University, Ukraine; e-mail: v_n_glushkov@yahoo.com*

Density functional theory (DFT) has emerged as a reasonably accurate tool for the calculation of ground state quantities. However, the successes of DFT have been clouded by its inability to deal satisfactorily with excited states (ES), especially ESs having the same spatial and spin symmetry as the ground state. It is known that DFT extension to excited states is neither unique nor straightforward. There exist distinct formulations and their number continues growing. Some of them, first proposed by Theophilou [1], rely on a variational treatment focusing either on ensembles or on an individual excited state approach [2]; others use non-variational approaches. But most of the practical calculations of excited states are nowadays carried out via time-dependent DFT (TD DFT), in which transition energies are obtained from the poles of dynamic linear response properties.

Recently a so-called constrained optimized effective potential (COEP) approach for excited states has been proposed [3,4]. This method is implemented within the framework of DFT for individual excited states and generates the Kohn-Sham excited state determinant which minimizes the total energy and is simultaneously orthogonal to the determinants for states of lower energies.

In this contribution we compare single excitation energies for small systems obtained by TD DFT method included in the package "GAUSSIAN" with those computed by the COEP method. We analyze a convergence of the results with respect to both exchange-correlation functional and basis sets using small atomic and molecular systems.

[1] A.Theophilou, *J.Phys.C. vol*. 12, 5419 (1979)
[2] M.Levy and A. Nagy, *Phys.Rev. Lett*. *vol.* 83, 4361 (1999).
[3] V.N.Glushkov, *Optics and Spectroscopy*, *vol*. 99, 684 (2005)
[4] V.N. Glushkov and M.Levy , *J.Chem.Phys*. *vol*.126, 174106 (2007)

Comprehensive DFT Investigation of 2'-Deoxyadenosine Adducts of *cis*-2-Butene-1,4-dial Formation

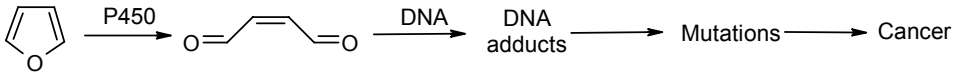
L. Sviatenko,[a,b] L. Gorb,[c] D. M. Hovorun,[c] J. Leszczynski[b]

[a]*Kirovograd State Pedagogical University, Kirovograd, 25006, Ukraine*

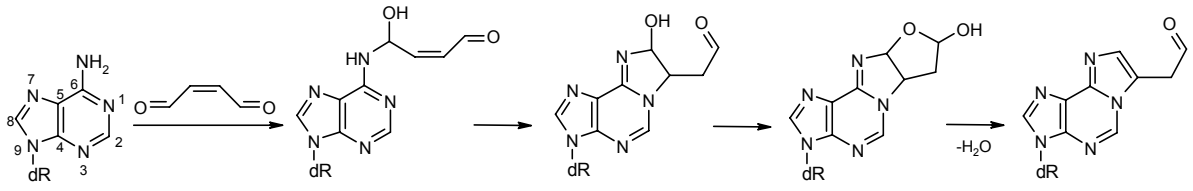
[b]*Interdisciplinary Nanotoxicity Center, Department of Chemistry and Biochemistry, Jackson State University, Jackson, Mississippi, 39217, USA*

[c]*Institute of Molecular Biology and Genetics, NAS of Ukraine 150 Zabolotny Str., Kyiv, 03143, Ukraine*

Furan is an important industrial product that is also found as pollutant in air, tobacco smoke, coffee, and canned foods. Metabolism of furan is catalyzed by cytochrome P450. It results in the formation of the α,*β*-unsaturated dialdehyde, *cis*-2-butene-1,4-dial, which reacts with a DNA to form mutagenic adducts and is thought to mediate furan's genotoxic effects. Despite of wide range of experimental studies the mechanism of *cis*-2-butene-1,4-dial interaction with DNA is not well-understood yet. Therefore, a characterization of a DNA modifications by furan is an important step in understanding both its toxicity and its carcinogenicity.



In this study the reaction pathway of 2'-deoxyadenosine with *cis*-2-butene-1,4-dial was investigated at the PCM/M05-2X/6-311+G* level of theory by simulating the equilibrium and activating thermodynamic parameters. Water molecules were involved as a catalyst. We have found that the reaction mechanism involves initial reaction of the C_1 atom of *cis*-2-butene-1,4-dial with the exocyclic nitrogen atom N_6 of dAdo. This event is followed by 1,4-addition of the adjacent endocyclic nitrogen atom N_1 of dAdo to the double bond of the remaining α,*β*-unsaturated aldehyde and subsequent attack of the alcohol on the second aldehyde group to form the isomeric primary products (**3**). Acidic catalyzed dehydration of primary products (**3**) leads to the final product (**4**).



1 **2** **3** **4**

Additionally, calculated UV and NMR spectra suggest that the primary and secondary 2'-deoxyadenosine reaction products represent hemiacetal forms of 3-(2'-deoxy-*β*-D-erthyropentafuranosyl)-3,5,6,7-tetrahydro-6-hydroxy-7-(ethane-2''-al)-9*H*-imidazo[1,2-α]purine-9-one (**3**) and 1''-[3-(2'-deoxy-*β*-D-erythropentafuranosyl)-3H-imidazo[2,1-i]purin-8-yl]ethane-2''-al (**4**), respectively.

QSAR study of thiazolidinone-pyrazoline conjugates which possessed promising anticancer activity *in vitro*

Dmytro Havrylyuk[a], Oleg Devinyak[b], Borys Zimenkovsky[a], Roman Lesyk[a]

[a]***Danylo Halytsky Lviv National Medical University, Lviv, Ukraine***

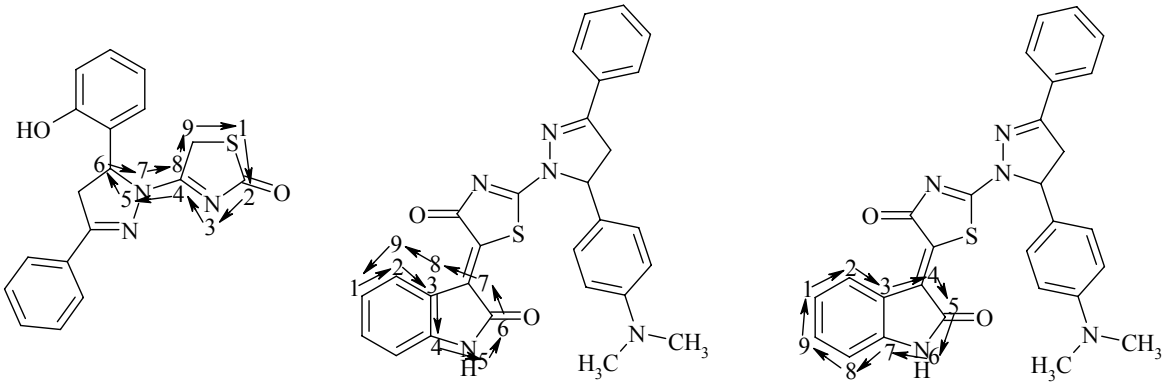
[b]***State Higher Educational Institution "Uzhgorod National University", Uzhgorod, Ukraine***

The combination of 4-thiazolidinone scaffold with other heterocycles is a widely applicable approach in a drug-like molecules buildup. The confirmation of this assertion could be various non-condensed systems with thiazolidine, diazole (pyrazoline or pyrazole) and related moieties that display broad spectrum of biological activities. A considerable interest has been focused on the anticancer activity of thiazolidinone and pyrazole derivatives. Among mentioned synthetic substances some of heterocyclic substituted 4-thiazolidinones were described in literature as inhibitors of necroptosis, Burkitt's lymphoma promotion or as promising agent, which possessed significant effect against breast carcinoma (MCF7) and cervix carcinoma (HELA) cell lines. The systematic study of 4-thiazolidinone derivatives with heterocyclic fragments in the molecules allowed us to identify a number of highly-active compounds *in vitro* as potential antitumor agents.

In the present work in continuation of an ongoing research we described the results of QSAR analysis of thiazolidinone-pyrazoline hybrids as promising anticancer agents.

Current modeling of anticancer activity was executed due to Organization for Economic Cooperation and Development (OECD) guidance and principles. The procedure of variance minimization for cancer growth percents obtained by two results of experimental studies in a defined endpoint. The best model was found by the check of all possible combinations of independent variables. Plotting standard errors *versus* leverages (Williams's graph) showed outliers and derives the domain of applicability. Goodness-of-fit was measured as Pearson's squared correlation coefficient and root mean squared error, robustness and predictivity were evaluated by means of internal and external validations. Additionally, response permutation testing (Y-scrambling) was carried out to estimate the probability of chance correlation.

Finally, the monoparametric QSAR model with squared correlation coefficient R^2=0.92 and Fisher's ratio F=362 have been obtained. The internal cross-validation showed explained variances (Q^2) for leave-one-out and leave-many-out (25%) procedures Q^2 = 0.90 and Q^2 = 0.91, respectively. The smaller explained variance for external validation (Q^2=0.82) indicated some overfitting, but further simplifying of monoparametric linear model was impossible. Y-scrambling test rejected the possibility of chance correlation. The robustness and good predictive power of the model were proved by the obtained statistical results. According to the current study, the inhibition of non-small lung cancer cells growth depends on the topological descriptor. It means that special mutual location of atoms in 2(4)-thiazolidinone structure define its anticancer activity.



The obtained results give the background for further directed syntheses of similar heterocyclic compounds with anticancer activity.

Reproducing acoustic relaxation kinetics in aqueous solution of human serum albumin by molecular dynamics simulations

T.O. Hushcha [a], S.O. Yesylevskyy [a,b]

[a] *Laboratory of Biomolecular Structure and Dynamics, Institute of Bioorganic Chemistry and Petrochemistry. Murmans'ka Street 1, Kiev-02094, Ukraine*

[b] *Department of Physics of Biological Systems, Institute of Physics, National Academy of Sciences of Ukraine. Prospect Nauki 46, Kiev-03039, Ukraine*

HSA is the prevalent constituent of human plasma protein. It has been shown to shuttle a broad range of endogenous and exogenous ligands including majority of known drugs. The search of structural basis for drug derivatives has stimulated general in silico calculations of HSA binding. Therefore, experimentally adjusted data on albumin flexibility and conformational dynamics is useful for development of computer-assisted drug design.

In this report we analyze dynamics of solvated HSA globule on a picosend to microsecond time scale, which is usually the most important for the functioning of proteins. We first combine two approaches, the experimental acoustic spectroscopy and MD simulations, to enable definite conclusions to be drawn regarding structure relaxation kinetics in HSA solutions.

Both acoustic and MD techniques can determine the rate of structural change in which the exponential return to equilibrium is observed after the variation of external pressure. Acoustic experiment monitors relaxation of molar volume resulting from periodically oscillating pressure when the sound wave propagates through protein solution. Constant pressure MD simulations can be used to calculate the relaxation of volume of solvated protein after a single-phase jump of pressure.

In this report the attempt is made to develop a consistent methodology of reproducing acoustic relaxation kinetics in MD simulations rather then detailed study of particular protein. We have performed the broadband (between 0,2 and 2000 MHz) measurements of the acoustic absorption spectra and have carried out extensive 175 ns MD simulations of volume relaxation in aqueous solution of HSA. We apply the same fitting algorithm in order to decompose relaxation curves obtained by two different methods into comparable kinetic components. We show that both acoustic and MD relaxation kinetics determined in this study for HSA solution may be represented within experimental and calculation errors by the set of components with discrete relaxation times. We find that relaxation times of all four components observed on nanosecond scale by both techniques match fine and can be attributed to solvated HSA. We consider two additional kinetic components observable in the picoseconds part of MD trajectory may obviously respond to bulk water. Also, in acoustic spectra we find two extra components exhibiting microsecond kinetics that may reflect aggregation of HSA globules.

We obtained remarkable agreement between the relaxation times in MD simulations and acoustic experiments. This agreement validates our protocol of the pressure jump in MD simulations and convinces us that the relaxations in the protein globule are the same in both cases despite the difference in methodology. This opens broad perspectives for interpreting the data of acoustic spectroscopy by means of MD.

Theoretical modeling of the interaction of G-quadruplexes with low-molecular ligands

M.M. Ilchenko, V.G. Kostina, I.Ya. Dubey

Institute of Molecular Biology and Genetics, National Academy of Sciences, 150 Zabolotnogo str., 03680 Kyiv, Ukraine; e-mail: m.m.ilchenko@imbg.org.ua

Telomeric DNA contains G-quadruplexes, specific structures formed by the stacks of guanine quartets. These formations play a key role in the control of telomerase activity. Telomerase enzyme is highly active in cancer cells, in contrast to normal ones where it is inactive. G-quadruplex structures of telomeric DNA are promising targets for the discovery of novel anticancer drugs. The unique structure of G-quadruplexes strongly differs from that of the other forms of DNA thus allowing their specific recognition by small molecules. Ligands that efficiently bind and stabilize G-quadruplexes are the inhibitors of telomerase activity and potential anticancer drugs.

The availability of crystallographic and NMR models of these macromolecular structures allows the development of new antitumor drugs by computational approaches. We have performed a model quantum-chemical study of complexes of G-quadruplex DNA with a number of low-molecular heterocyclic ligands.

All calculations have been performed by DFT method using M06, M062X and WB97XD functionals, and semi-empirical PM3-D method [1], with software packages Gaussian 09 provided by the Mississippi Center for Supercomputing Research, USA [2], and GAMESS-US installed on the SCIT-3 complex at the Glushkov Institute of Cybernetics, NAS of Ukraine [3].

The first step of this study was a theoretical search for the adequate models of the binding centers of various classes of G-quadruplex ligands. Natural G-quadruplexes formed by the specific folding of guanine-rich polynucleotide sequences seem to be too complex structures for the direct application of quantum-chemical methods. We have developed a convenient model of G-quadruplex. It is guanine octet consisting of a coplanar pair of Hoogsteen hydrogen-bonded guanine quartets stabilized by stacking and π-π interactions and containing an ammonium cation located between the quartet planes. This is a simple model of G-quadruplex DNA structure consisting usually of three or four stacked deoxyguanosine quartets.

In order to analyze the utility of the proposed model, a number of structures have been screened including some representative G-quadruplex binders (telomestatin, berberin and cationic tetra(N-methylpyridinium)porphyrin TMPyP) and a series of new acridone derivatives synthesized in our laboratory. The interaction of the model guanine octet with these molecules has been investigated to determine binding energies and geometries of ligand-octet complexes. It has been shown that the calculated interaction energies of G-octets with tested ligands directly correlated with their biological activity. Our investigation have resulted in the identification of several small molecules that efficiently bind to G-quadruplex DNA.

Thus we have developed a simple and convenient model for the quantum-chemical screening of G-quadruplex ligands. Molecular modeling results can be applied for the design and synthesis of new selective and potent G-quadruplex-mediated telomerase inhibitors with anticancer activity.

[1] Stewart, L. Fiedler, P. Zhang, J. Zheng, I. Rossi, W.-P. Hu, G.C. Lynch, Y.-P. Liu, Y.-Y. Chuang, J. Pu, J. Li, C.J. Cramer, P.L. Fast, D.G. Truhlar. MOPAC–version 5.016mn, University of Minnesota, Minneapolis, MN 55455.

[2] http://www.mcsr.olemiss.edu

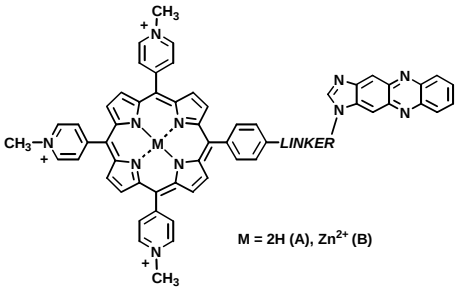
[3] https://icybcluster.org.ua

Molecular structure of TMPyP-imidazophenazine conjugates

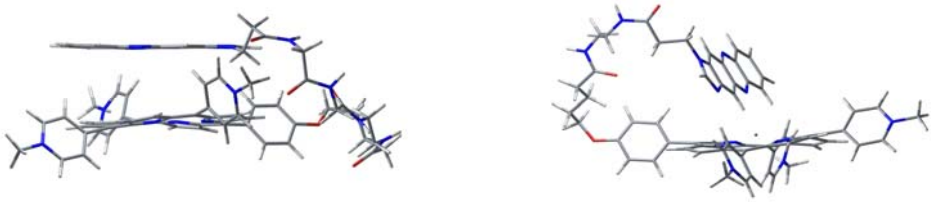
M.M. Ilchenko, L.V. Dubey, I.Ya. Dubey

Institute of Molecular Biology and Genetics, National Academy of Sciences, 150 Zabolotnogo str., 03680 Kyiv, Ukraine; e-mail: m.m.ilchenko@imbg.org.ua

Compounds that specifically bind to G-quadruplex structures of telomeric DNA are known to inhibit telomerase and exhibit antitumor properties. In the course of our studies on the design of G-quadruplex ligands we have synthesized a series of conjugates of the classic quadruplex binder, porphyrin TMPyP and its metal complexes, with a neutral intercalating agent imidazophenazine (ImPhz) linked via various polyamide linkers, and demonstrated their antiproliferative activity [1]. The spectral-fluorescent studies of TMPyP-ImPhz hybrids (e.g. fluorescence quenching data) suggest the formation of rather stable complexes between the two chromophores. To check this assumption we have performed a quantum-chemical study of the conjugate structures.



All calculations have been carried out with Gaussian 03/09 packages installed at the Mississippi Center for Supercomputing Research [2] by DFT method using M06 and M062X functionals that adequately describe stacking interactions, and 6-31G(d) and 6-31G(d, p) basic sets. Full geometry optimization has been performed in vacuum and in water; we have employed supermolecular approximation and PCM model to consider the solvent effects. The equilibrium geometry has been studied to demonstrate the formation, both in vacuum and water, of intramolecular complexes where ImPhz directly interacts with a porphyrin moiety. Two structures are realized depending on the presence of metal cation in the porphyrin ring. Non-metalated conjugates (A) adopt the conformation with coplanar chromophores stabilized by stacking interactions. For Zn(II)-porphyrin (B), the metal coordination with a central nitrogen atom of ImPhz fragment results in the formation of the other type of complex where the chromophores are perpendicular to each other.



A **B**

The structure of the linker between chromophores has quite limited effect on the process. The folding of the linear conjugate resulting in the binding of ImPhz fragment to the porphyrin residue is energetically very favourable. For example, for Zn(II) complex ΔG_{298} of the process in vacuum and water is 15.61 and 12.34 kCal/mol, respectively. So the solvent does not significantly affect the formation of intramolecular complex.

Thus quantum-chemical methods have shown that cationic porphyrin conjugates with polycyclic heteroaromatic compounds like imidazophenazine can form intramolecular complexes due to either stackimg interaction or metal cation coordination with a nitrogen atom of the conjugated molecule, fully confirming experimental data on the tendency of these conjugates to form the head-to-tail type complexes.

[1] L.V. Dubey, V.N. Zozulya, O.A. Ryazanova, I.Ya. Dubey. Manuscript in preparation.
[2] http://www.mcsr.olemiss.edu

Evaluation of the Lewis Acidity of organoboron compounds. Quantum chemical descriptors based on the electron density

Michał Jakubczyk, Agnieszka Adamczyk-Woźniak, Andrzej Sporzyński

Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3 Str. 00-664, Warsaw, Poland; e-mail: mjakubczyk@ch.pw.edu.pl

Nearly all organoboron compounds are considered strong organic Lewis acids, what makes them useful in many applications as: polymer electrolytes additives[1], catalysts[2], electrophiles in organic synthesis etc. Boronic acids are one of the most popular subject in organoboron chemistry.

It's well known that the Lewis acidity of the boron atom in phenylboronic acids is increased upon ester formation. Esters with simple diols were found to be very useful in the above applications and are easy to obtain by reaction of an acid with diol. The Lewis acidity of the boron center depends on the type, number and position of the substituents in the phenyl ring. However, the structure of the diol residue was found to be crucial for the Lewis acidity of the ester.

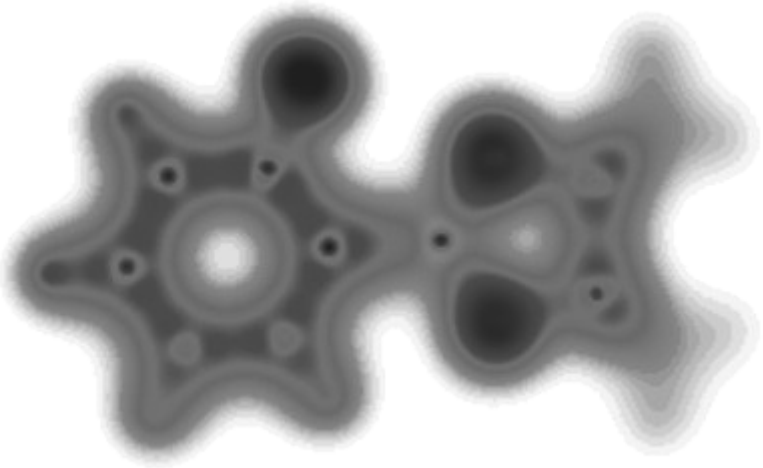


Figure: Laplacian of the DFT-calculated density of pinacol 2-fluorophenylboronate.

This work is an attempt to explain in detail the influence of the diol structure on the Lewis acidity of phenylboronates. A series of ring-fluorinated phenylboronic esters was synthesized. Their Lewis acidity towards Et_3PO was measured by ^{31}P NMR spectroscopy[3] and calculated using DFT-GIAO method. The topology of the calculated electron density was analyzed in terms of the ESP (electrostatic potential) and the Laplacian.

[1] M. Marcinek, G. Z. Żukowska, W. Wieczorek, *Electrochim. Acta* **2005,** 50, 3934-3941.
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[3] U. Mayer, V. Gutmann, W. Gerger, *Monatsh. Chem.* **1975**, 106, 1235-1257.

The calculations reported in this work were partially performed at the Interdisciplinary Center for Mathematical and Computational Modeling of the University of Warsaw within grant No. G36-20. Financial support within grant No. N N 204127938 is kindly acknowledged.

Density Functional Theory Study of Defected BC_3 Nanotubes

S. Jalili

Department of Chemistry, K. N. Toosi University of Technology, Tehran, Iran

Defects, which are formed during the growth of carbon nanotubes (CNTs), or may be triggered by ion irradiation or external mechanical forces, may influence the physicochemical properties of CNTs and their binding affinity for adsorbed molecules. We have studied the structural defects, such as 5–7–7–5 Stone–Wales (SW) defect and single vacancy in a (4,0) BC_3 nanotube. We have employed density functional theory (DFT) geometry optimizations using plane waves and pseudopotentials to study the formation energy and reconstruction of defects in the walls of a BC_3 nanotube. Seven types of structures have been optimized, including a perfect nanotube, four types of SW defects (corresponding to the rotation of axial and circumferential C−C and C−B bonds), and two single vacancies (V_C and V_B). For the structure with a V_B defect, spin-polarized calculations were performed. The most stable structures was obtained and compared to the results for CNTs.

[1] Y. Miyamoto, A. Rubio, S. G. Louie, M. L. Cohen, *Phys. Rev. B*, **50**, 18360 (1994).
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[3] S. Jalili, A. Vaez, *Chem. Phys. Lett.*, **437**, 233 (2007).
[4] S. Berber, A. Oshiyama, *Physica B*, **376−377**, 272 (2006).

Theoretical investigation of spectral-luminescent properties of some polymethine bis-chromophores

E.R. Kashapova, V.Ya. Artyukhov, G.V. Mayer

Tomsk state university, Lenin str., 36, Tomsk, Russia

In the work results of theoretical research of spectral-luminescent properties in monomer of indocarbocyanine (A-1) and its bis-derivatives in which two chromophores are connected by one (A-2, A-3- angular dimers) and two (A-4, A-5 - cyclic dimers) chains consisting of various number of methylene groups are presented. The structure of the investigated molecules is shown on fig. 1. Bis-cyanines, in comparison with monomers, demonstrate changes in absorption and fluorescence spectra which are typical for dimers, as a result of S_1-level splitting into levels with high and lower energy (the Davydov splitting). One may expect a difference in photophysical properties between monomeric and covalently linked dimeric cyanines. Dimers may be considered as the simplest associates in the course of the formation of higher aggregates, which are formed when the dye concentration is increased; dimerization is usually considered as the first step of aggregation. The study of aggregates may meet some difficulties when interpreting the results due to different aggregation numbers and because in solution the equilibria exist between aggregates of different compositions including those with monomers. Bis-chromophores which are monomeric forms in reasonably diluted solutions are free from these disadvantages [1].

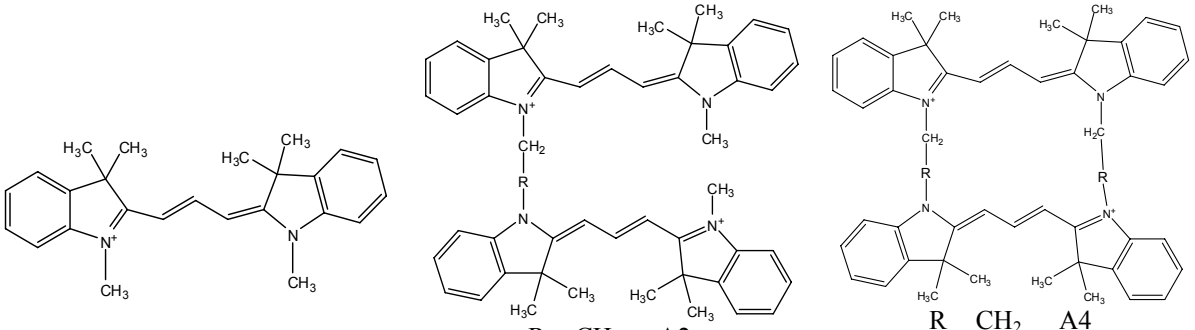

Fig. 1. Structure of molecules under investigation

Calculations were carried out with use of semiempirical method of intermediate neglect of differential overlap (INDO) with spectroscopic parameterization [2], TDDFT method and CIS method [3, 4]. All calculations were carried out with use of the geometry received from X-ray data for a related class of compounds. Rate constants of photophysical processes, the quantum yield of fluorescence from the first singlet state were estimated by INDO method.

It is established that the reason of a low quantum yield in cyclic bis-cyanines is a reduction of a rate constant of radiation decay by two order and an increase of a rate constant of internal conversion, the rate constant of intersystem crossing increases in comparison with that for a monomer, but still can't compete to a rate constant of internal conversion.

Work is executed with support of The Federal Target Program (contracts № П 1128, № 02.740.11.0444) and the grant of the President of the Russian Federation (НШ-4297.2010.2).

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Interaction of bioactive ferulic and caffeic acid with fumed silica

O.A. Kazakova, N.A. Lipkovska, T.V. Kulik, V.N. Barvinchenko, B. B. Palyanytsya

O.O.Chuiko Institute of Surface Chemistry National Academy of Sciences of Ukraine, 17 Gen. Naumov str., Kyiv, 03164, Ukraine

Medicinal plants are the richest bio-resource of drugs of both traditional and modern medicines. Plant-derived polyphenols, in particular, phenolic acids have recently become of great interest owing to their various therapeutic properties. Thus, cinnamic acid (C_6H_5–CH=CH–COOH) and its hydroxy-derivatives, e.g. 3- methoxy-4- hydroxy-cinnamic acid (ferulic acid, Fer) and 3,4- dihydroxy-cinnamic acid (caffeic acid, Caf) were found to exhibit high bioactivity. The fumed silica is effectively used in medical practice as an entherosorbent, composite component and a carrier of herbal and synthetic remedies**.**

The aim of this work was to study the properties of biologically active ferulic and caffeic acid and its adsorption mechanism on the silica surface.

Structural and electronic characteristics of Fer and Caf molecules and model clusters of silica $Si_{12}O_{30}H_{12}$, the interaction energy of acid molecules with the silica cluster were calculated using Hartree-Fock theory with the 6-31G(d) basis set by means of the GAMESS (current versions). The solvation model SM5.42 (GAMESOL program package, Version 3.1 based on GAMESS) were used to study the solvent effects for molecules, clusters, and their complexes.

Different functional groups in Fer and Caf molecules, i.e. several reaction centers make possible the formation of different energetically favorable surface complexes on silica surface. Their proportion depends on the free energy of the formation and experimental conditions. It was found that the most energetic surface complex is formed via the nondissociated phenolic hydroxyl groups of acids and observed experimentally for all the samples obtained in different ways – silica loading by adsorption, mixing and co-milling. Formation of the surface complex via Fer and Caf carboxyl group was found for the samples with a high surface coverage (60–600 μmol/g) obtained by mixing and co-milling. In all cases the concentration of the complex formed via phenolic group is 3-4 times more than that formed via a carboxyl group.

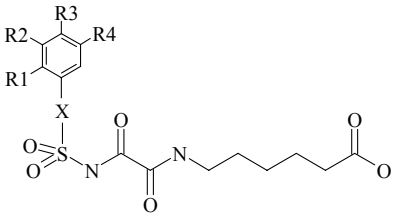
Predictive QSAR modeling of Diuretic Activity for 6[([phenyl]sulfonylamino)-(oxo)acetyl]aminohexanoic acid derivatives Using 3D Molecular Descriptors

O.V. Klenina[a], A.A. Cepelevski[b], V.V. Ogurtsov[a], I. Ya. Golos[a]

[a] *Danylo Halytsky Lviv National Medical University, 69 Pekarska Str., Lviv, 79010 Ukraine*

[b] *National pharmaceutical university, 53 Pushkinska Str., Kharkiv 61002, Ukraine*

3D molecular descriptors combined with appropriate weighting schemes are highly sensitive to the 3-dimentional molecular structure, allow to compare molecular conformers taking into account their shape, size symmetry and atom distribution and seems to indicate a connection between the molecular structure of substances and their biological activity. In this study, 3D-descriptors were used to predict diuretic activity for a series of 21 compounds 6-[([phenyl]sulfonylamino)-(oxo)acetyl]aminohexanoic acid derivatives possessing significant diuretic activity (the Berxin's test on rats, %). Furocemide, hydrochlorothiazide and metamizole sodium were used as standards.



X = CH_2 or none
R_1 = H, Br, NO_2 **R_2** = H, NO_2, COOH
R_3 = H, CH_3, COOH, NH_2, NO_2, Cl, Br, OCH_3, $COOCH_3$, $COOC_2H_5$, CH_2NH_2, $NHCOOCH_3$, $CH_2NHCOCH_3$, $NHCONHC_6H_{11}$(cyclo)
R_4 = H, Cl, Br

Firstly geometry optimization of compound using semi-empirical PM3 method using the Polack-Rabiere algorithm included in HyperChem 7.5 software was carried out.

The DRAGON software web version 3.0 was employed to calculate the conformational (3D) molecular descriptors of five kinds: Geometrical Descriptors, RDF (Radial Distribution Function), 3D-MoRSE (3D Molecule Representation of Structures based on Electron diffraction), WHIM (Weighted Holistic Invariant Molecular) and GETAWAY (GEometry, Topology, and Atom-Weights AssemblY). MLR analysis implemented in BuildQSAR software with stepwise selection and elimination of variables was employed to QSAR-modelling with different types of descriptors separately. The GA was used as the variable selection strategy. In order to avoid collinearity, Randic orthogonalization procedure was carried out. The individual descriptors revealing the most significance were used for QSAR mixed models operation. Regression models predictive power was validated by calculating Q^2. The statistical significance was determined by the regression correlation coefficient r, the Fischer ratio F and the standard deviations. Obtained one-, two- and three-variables mixed modes contain 2 negatively contributing (HOMA, HOMT) and 1 positively contributing (QZZ*m*) Geometry Descriptors, 1 positively contributing RDF (RDF075*m*) and 10 GETAWAY molecular descriptors: H5*e*, H5*u*, R7*e*, R1*e*+, R3*e*+ (positively contributing, the regression coefficients reveal the most significance of the last one) and REIG, HATS2*u*, HATS4*e*, R1*p*, R2*p* (negatively contributing, REIG being of the most significance). The correlation coefficients r increase with the number of variables been increased: 0.716-0.717 for one-, 0.800÷0.840 for two-, and 0.904÷0.927 for three-variables models. Q^2 increases in the same manner: 0.289-0.290, 0.431÷0.552 and 0.708÷0.744, respectively. F=15.983÷34.444 for obtained mixed models. The proposed QSAR approach based on 3D molecular descriptors using may be purposeful for the further synthesis strategy development of novel aminohexanoic acid derivatives as potential diuretic drugs.

A density-functional study of oxygen adsorption on binary platinum-cobalt nanoclusters

V.I. Pokhmurskii, S.A. Korniy

Karpenko Physico-Mechanical Institute of the National Academy of Sciences of Ukraine, 5, Naukova Str.,79060, Lviv, Ukraine; e-mail: kornii@ipm.lviv.ua

The binary platinum nanoclusters with transition metals have been widely proposed as perspective catalytic materials for electrodes of low temperature fuel cells. Such compounds possess enhanced catalytic activity when compared with pure metals. Besides such nanoclusters of platinum include transition metals, where oxygen adsorption is irreversible and strong chemical bonds are formed and a catalytic corrosion occurs with the destruction of the nanoclusters. Thus the objectivities of the present study were calculations of oxygen adsorption heats and activation energies on the surface (111) of platinum-cobalt binary nanoclusters on the basis of quantum-chemical methods in a cluster approximation.

Binary nanoclusters were constructed by substitution of both atoms for initial icosahedral nanocluster Pt_{55}. Two species of $Pt_{37}Co_{18}$ nanoclusters were calculated – a «core-shell» structure, where exclusively platinum atoms are situated at the surface, while cobalt atoms formed the cluster core, and proportional structure, the cobalt content of which was almost 50%. The electronic structure of nanoclusters was calculated by means of quantum-chemical program StoBe 2008 [1] in generalized gradient approximation (GGA) for exchange correlation functional B88-LYP and double-zeta valence polarization DZVP basis set of the implemented functional density theory DFT.

The results obtained are in satisfactory agreement with experimental data about the enhanced catalytic activity of binary nanoparticles based on platinum and cobalt. Such enhanced activity of binary nanoclusters in the «core-shell» model is connected with reaction ability of surfaces to oxygen reduction as well as with the strength of chemical bond between the surface and atomic oxygen. This determines both catalytic and corrosive resistance of binary nanoclusters. Thus the activation energy of O_2 adsorption at the surface of binary nanocluster $Pt_{37}Co_{18}$ is higher almost for all adsorption sites as compared with pure Pt_{55} and binary nanocluster $Pt_{37}Co_{18}$ with the proportional composition (1.23 eV for $Pt_{37}Co_{18}$ (the «core-shell» model) and 0.97 and 0.21 eV for Pt_{55} and $Pt_{37}Co_{18}$ (the proportional model) respectively). This indicates about the higher possibility of O_2 dissociation rather its chemisorption. The strength of oxygen bond with nanocluster surfaces is determined by adsorption heats and the calculated value is lower at the $Pt_{37}Co_{18}$ surface in the «core-shell» model (during adsorption of O_2 – 0.51 eV for $Pt_{37}Co_{18}$ (the «core-shell» model) and 0.54 eV and 1.16 eV for Pt_{55} and $Pt_{37}Co_{18}$ (the proportional model) respectively; under adsorption of O – 3.38 eV for $Pt_{37}Co_{18}$ (the «core-shell» model) and 3.67 eV and 4.65 eV eV for Pt_{55} and $Pt_{37}Co_{18}$ (the proportional model) respectively). Therefore our binary $Pt_{37}Co_{18}$ nanocluster of the «core-shell» model has the lower affinity to oxidation.

Thus binary nanoclusters based on platinum with the «core-shell» structure possess enhanced catalytic activity and higher stability to oxide formation during their action in the electroreduction reaction at the cathodes of low temperature fuel cells.

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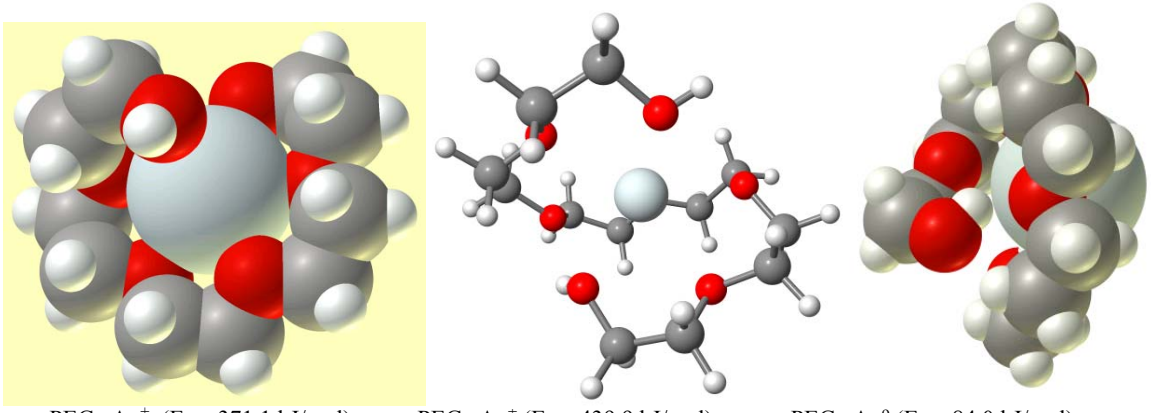
DFT Study of Ag^+ and Ag^o Clusters with Poly(ethylene glycol) Oligomers

M.V. Kosevich, V.V. Chagovets, S.G. Stepanian

B. Verkin Institute for Low Temperature Physics and Engineering of the NAS of Ukraine, 47 Lenin Ave., Kharkov 61103, Ukraine; e-mail: mvkosevich@ilt.kharkov.ua

In contrast to relatively stable composites of poly(ethylene glycol) (PEG) with alkali metal salts used as polymeric electrolytes, systems composed of PEG and silver salt $AgNO_3$ are used in up-to-date nanotechnology for production of silver nanoparticles via Ag^+ ions reduction [1]. In our experimental mass spectrometric studies of (PEG-400 + $AgNO_3$) system abundant $PEG_n•Ag^+$ clusters (where n is the number of monomers in the PEG chain) were observed along with silver nanoclusters Ag_m^+. In the present work we have performed a simulation of $PEG_n•Ag^+$ and $PEG_n•Ag^o$ (n = 5, 6) complexes aimed at elucidation of some features of silver behaviour in the polyether medium. DFT/B3LYP method with 6-31++G** basis set for the oligomers and Stuttgart RSC 1997 ECP set for silver was applied.

It was revealed that in $PEG_n•Ag^+$ complexes PEG oligomers form quasi-cyclic and quasi-helical structures around the Ag^+ ion, similarly to the structures of PEGs in their associates with alkali metal ions well known from the Literature.



$PEG_5•Ag^+$ (E = -371.1 kJ/mol) $PEG_6•Ag^+$ (E = -439.9 kJ/mol) $PEG_6•Ag^o$ (E = -84.0 kJ/mol)

The ether oxygen atoms of the polyether chains and terminal OH-groups coordinate the centered Ag^+ cation in $PEG_n•Ag^+$ complexes. The wrapping of the neutral metal atom by the chain is preserved in the $PEG_n•Ag^o$ complexes, which agrees with the data reported earlier for silver atom complexes with crown ethers [2], although OH-groups change their orientation. Since the radius value of Ag^+ (0.126 nm) is close to those of Na^+ (0.095 nm) and K^+ (0.133 nm), the earlier obtained structural data for PEG_n-alkali ion complexes could be extrapolated to $PEG_n•Ag^+$ ones whilst the electrostatic interaction only is concerned. The difference between the PEG complexes with Ag^+ and with alkali metal ions is revealed at the level of the frontier orbitals analysis. While in $PEG_n•Na^+$ and $PEG_n•K^+$ complexes LUMO is located at the polymer only, in $PEG_n•Ag^+$ it is distributed over both the oligomer and Ag^+. This means that the silver ion preserves its ability to capture electrons (that is to be reduced) in such complexes.

The data obtained will be used in further simulation of PEGylated inorganic nanoparticles of silver.

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A computational DFT study of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones tautomeric forms

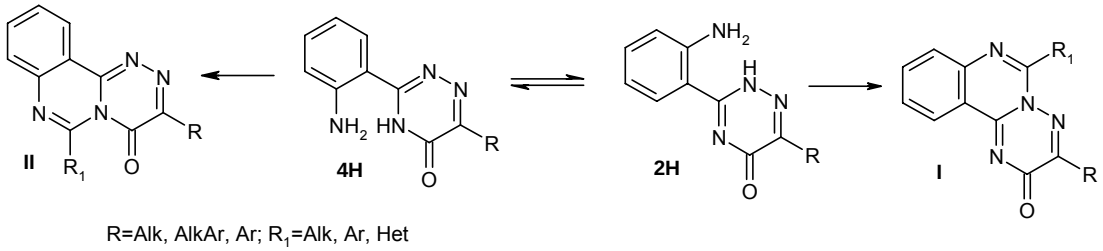
Kovalenko S.,[a] Okovytyy S.,[b] Berest G.,[a] Voskoboynik A.,[a] Skorina D.[a]

[a] *Zaporozhye State Medical University, Ukraine; e-mail: kovalenkosergiy@gmail.com*

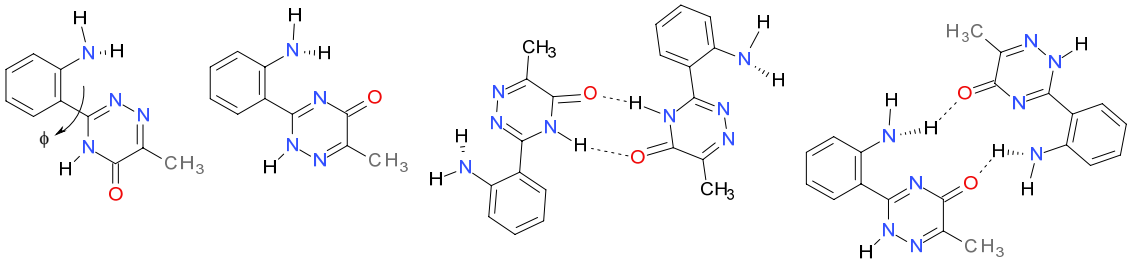
[b] *Dnepropetrovsk National University named after Oles Honchar; e-mail: sokovyty@icnanotox.org*

6-R-3-(2-Aminophenyl)-1,2,4-triazin-5-ones (**1**) are functional 1,5-NCCCN-binucleophiles able to exist in two tautomeric forms (2*H*, 4*H*) due to prototropic tautomerism caused by presence of imide bond in 1,2,4-triazine cycle. Interaction of mentioned tautomeric forms with dielectrophyles (heterocyclisation reaction) may lead to formation of corresponding 6-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazoline-2-ones (**I**), or isomeric 6-substituted 3-R-2*H*-[1,2,4]triazino[4,3-*c*]quinazoline-2-ones (**II**, scheme). Biological activity of compounds **I** and **II** are insufficiently investigated, among them are perspective antidepressant, antihypoxant, cardioprotective, antiinflammatory, analgetic, antibacterial and anticancer agents.

Scheme



Here we present the results of quantum-chemical investigation of thermodynamic stability of of 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (**1**) tautomeric forms obtained with density functional theory at M062X/cc-PVDZ level of theory. Solvent effects have been taken into account using PCM approach. According to calculations in the row of monomeric forms the most stable one is 4*H* tautomer, while formation of dimer significantly stabilizes system due to formation of two N-H···O hydrogen bonds (dimerization energy for tautomer 2*H* equals to 11.15 kJ/mol). Such stabilization results in displacement of equilibrium into formation of 2*H* dimer in 94.41%.



	2H	**4H**	**2H dimer**	**4H dimer**
ϕ	25.0^0	28.1^0	22.1^0	29.5^0
ΔG_{rel}	2*(**2H**) 11.15 kJ/mol	2*(**4H**) 7.63 kJ/mol	0.00 kJ/mol	27.89 kJ/mol
Population	1.05 %	4.34 %	94.41 %	<0.01 %

Obtained results were in agreement with experimental data, according to which corresponding 6-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones (**II**) were the single products of interaction between 6-R-3-(2-aminophenyl)-1,2,4-triazin-5-ones (**1**) with carboxylic and dicarboxylic acids anhydrides in DMFA and acetic acid. The structure of new 6-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones **II** was elucidated by means of single-crystal X-ray analysis (www.ccdc.cam.ac.uk/data_request/cif) and confirmed by spectroscopic investigations.

Quantum-chemical research of the de-NOx SCR reaction on the surface of vanadium dioxide

Maxim Kukuev [a], Victor Lobanov [b], Vitaliy Yazimirskij [a]

[a] *Taras Shevchenko Kyiv National University, 01033, Kyiv, Volodimirska str. 64; e-mail: last_of_west@inbox.ru*

[b] *Chuiko Institute of Surface Chemistry of the National Academy of Sciences of Ukraine, 03164, Kyiv, Generala Naumova str., 17*

Preservation of the natural environment and therefore elimination of pollutants has becomes a major concern in the present world. Selective catalytic reduction (SCR) of nitric oxide by ammonia over vanadium oxide based catalysts is the most technically advanced post-combustion technology capable of reducing NO_x emissions. Although the numerous experimental studies carried out, a complete elucidation of the reaction mechanism has not been achieved.

The "classic" catalyst for such a reaction in industry is V_2O_5 supported on anatase. As concluded by some authors, it works best if the vanadium oxide coverage is slightly less, then a monolayer. In the other hand there are reports about successful epitaxial growing of V_2O_5 on titania surface. At low coverages vanadium oxide have structure similar to material of support – rutile or anatase. In the case of anatase oxidation state of vanadium is +5, in the case of rutile – more common material, estimated oxidation state is +4, and vanadium oxide follows rutile structure since a rutile-structured phase is the lowest energy form of VO_2.

The oxidation state of the active site is uncertain. This is due to the complexity (heterogeneity) of the system. V_2O_5 could be reduced to become active. According to DRIFTS experiments, the reduced oxide is more effective than the oxidized oxide. The reduction of NO in absence of NH_3 has been reported over V_2O_4 catalyst. NO adsorption has been reported to occur exclusively on reduced vanadia. For the SCR catalyst, EPR signals show the presence of antiferromagnetic d^1-d^1 ion pairs such as V^{4+}-V^{4+}. Some experiments assign an oxidation state of +4.4 for the vanadium centers in SCR conditions.

Present study is concern with VO_2 surface. Cluster was modeled by means of B3LYP DFT method. Some aspects of numerous proposed reaction mechanisms of SCR reaction were investigated. The GAMESS10 program has been used for modeling of solid cluster to receive the energetic parameters that are close to experimental results. The research of mechanism have been realized by energetic effects analysis of elementary stages and choosing the energetically efficient reaction way. The cluster has been modeled as surface (011) VO_2 fragment. The molecules, intermediates, energetic parameters of their interaction have been investigated.

The quantum-chemical research of the chemisorptions during the silica surface modification

Kukueva V.V.

Academy of Fire Safety, 18034, Onoprienko str. 8, Cherkassy, Ukraine; e-mail: kukueva@yahoo.com

The quantum-chemical research for alternatives to halon fire suppressants has to date produced any candidates, that meet all the criteria for next generation fire suppressants. The following chemical families are likely to contain chemical substances, which have both properties: a high degree of fire suppression efficiency and low environmental impact: the bromoalkenes, fluoroakanes, and phosphorus-containing compounds, including the alkyl phosphates, phosphates and phosphonates. [1]. All of choosing chemical families representatives have been researches by means quantum-chemical calculations on the level of elementary interaction between active centers of flame and destruction products of fire suppressants. As well known adsorption is a process where molecules from the gas phase or from solution bind in a condensed layer on a solid or liquid surface. The nature of bonding between adsorbate and surface is still subject to some interpretation. On a more fundamental level, when a molecule is chemisorbed, the electrons are shared between the adsorbate and the surface. As a result, the adsorbate's electronic structure is significantly perturbed. The surface's electronic srtructure is perturbed to a lesser extent. So, a molecule is chemisorbed if the molecule's electronic structure is significantly perturbed upon adsorption. Typical chemisorptions energies are 15-100 kcal/mole for simple molecules. As far as have been shown in our previous papers [2] immobilization of active inhibiting components on the silica surface could improve their catalytic activity.

The quantum-chemical calculations have been provided by the *ab initio* method in the 6-31 basis set to investigate the chemical way to destruct of organic molecules immobilizing on the silica surface. Because the point defects, stabilized on the activated silica surface has the high reactivity, and they have been used as "foundation" for immobilized on the surface intermediates. Calculations have been provided both for the isolated molecule and for the immobilizing one on the silica surface. The calculation results have presented in the table.

Abstraction from the silica surface	$E_{destr.\ bind.}$ (kcal/mol)	Abstraction from molecules	$E_{destr.\ bind.}$ (kcal/mol)
$[(OH)_3Si\ \ldots CF_3]$	61,21	$CHFCl - CF_3 \rightarrow CHFCl\bullet + CF_3\bullet$	73,0
$[(OH)_3Si\ \ldots Cl]$	54,61	$CHFCl - CF_3 \rightarrow CFH\bullet - CF_3 + Cl\bullet$	68,98
$[(OH)_3Si\ \ldots F]$	28,99	$CHFCl - CF_3 \rightarrow CHCl\bullet - CF_3 + F\bullet$	65,15

As we can see from the table, the more preferable destruction way from the silica surfaces for all of researched radicals. It is surprisingly, that presence of fluorine atom increases of the bind strength. It could be connected with high electronegativity and less radius of Florine. All of these predictions are coinciding with experimental observations and spectroscopic data.

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QSPR study of drugs bioavailability

M. A. Kulinskiy, I.Yu. Borisuk, A.G. Artemenko, P.G. Polischuk, V.E. Kuz'min, N.Ya. Golovenko

A.V.Bogatsky Physico-Chemical Institute of the National Academy of Sciences of Ukraine, 86 Lustdorfskaya doroga, Odessa 65080, Ukraine; e-mail: docmax@inbox.ru

Bioavailability is one of the most important pharmacokinetic characteristics of the drugs and is typically defined as a fraction of an administered dose of unchanged drug that reaches the systemic circulation. The bioavailability of a drug is an important attribute that is investigated early in drug development and used throughout development. In many cases, it is the deciding factor as to whether or not a drug candidate is selected for further development. Intravenous bioavailability is always 100%. Oral bioavailability is usually less than 100% due to incomplete absorption in the gastrointestinal tract and first-pass metabolism in the liver.

Thus, the aim of the present work is developing QSPR models of oral bioavailability of various drugs. The final modeling dataset included more than 600 structurally diverse drug substances, e.g. zanamivir, amprenavir, paracetamol, nitrazepam, butabarbital, furosemide, alprenolol, etc.

For solution of QSPR tasks the Hierarchical QSAR Technology (HiT QSAR) based on Simplex representation of molecular structure (SiRMS) was used. In the SiRMS approach a molecule is represented as a system of different simplex descriptors (tetra atomic fragments with fixed composition, structure, chirality and symmetry). The key feature of the SiRMS approach is the use of sundry variants of differentiation of simplex vertexes (atoms) at the stage of simplex descriptor generation, such as: 1) atom type; 2) partial atom charge 3) lipophilicity; 4) atomic refraction 5) donor/acceptor of hydrogen in the potential H-bond; etc.

In this study, QSPR models were developed based on 2D level of simplex descriptors using Random Forest (RF) statistical approach. Predictions for external datasets and designed/screened compounds were made using consensus scheme, i.e., by averaging predictions generated with multiple validated training set models. All the compounds from the dataset were divided into three (low, moderate and high) or two (high and acceptable) bioavailability classes. For each classification several QSPR models were developed. The classification of two classes had better predictive ability than three class classification models. Taking into account varying of bioavailability in some range of values, in the two class models we have introduced a confidence interval (10% of the range) between two classes. The predictition error in obtained classification QSPR models was about 15%.

Docking studies and molecular design of 4-thiazolidinone derivatives as potent Bcl-X_L inhibitors

Vasyl' Atamanyuk, Olexandra Hrabous, Roman Lesyk

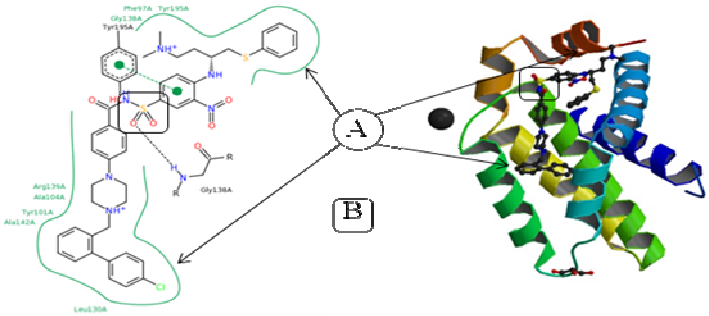
Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Bcl-X_L an antiapoptotic member of the Bcl-2 family. Located at the outer mitochondrial membrane and regulates outer mitochondrial membrane channel (VDAC) opening. VDAC regulates mitochondrial membrane potential, and thus controls the production of reactive oxygen species and release of cytochrome C by mitochondria, both of which are potent inducers of cell apoptosis. Overexpression of this protein is reported in all types of cancer cells that provides a target for directed search of inhibitors among 4-thiazolidinone derivatives. 4-Thiazolidinones are well-known class of substances that is related with a wide spectrum of biological activity and usage as pharmacological agents. This class of compounds possesses hypoglycaemic, antimicrobial, anti-inflammatory, choleretic, antitumor, diuretic, immunostimulant, and recently, attention has been paid to the antineoplastic activity of thiazolidinone derivatives [1].

Our aim was to build structure-based combinatorial library of 4-thiazolidinones derivatives and to select a proper sub-library for synthesis, using ranking of their docking scores.

Docking studies were performed with OpenEye Scientific Software program package that include Fred Receptor, Vida, Flipper, Babel3, Omega2 and Fred. The molecular docking included the following stages: [a)] generating R-, S- and cys-, trans-isomers of ligands using program Flipper, [b)] 3D optimization of isomers using program HyperChem 7.5 (www.hyper.com) (molecular mechanics method MM+ with following semi-empirical quantum-mechanical method PM3), [c)] conformers generation (Omega2) and [d)] 3D molecular docking (Fred). Up to date Protein Data Bank (www.rcsb.org) contain complexes of Bcl-X_L with sulfonamide inhibitors, particulary models 3QKD, 3INQ, 2YXJ, 2O21, 2O22, 2O2F, 2O2M, 1YSI, 1YSN, 1YSX (PDB ID's). For studies was selected complex 2YXJ (Bcl-X_L with ABT-737) because of it's highest resolution (2,2Å) of crystallographic model. According to crystallographic data [2] were identified molecular fragments crucial for high binding affinity with protein:

A) Hydrophobic fragments in pockets p2 and p4
B) Sulfonamide group (H-bond acceptor) that forms hydrogen bond



According to this data combinatorial library was built containing 1,500 molecules – 4-thiazolidinone derivatives and 16000 molecules from ZINC database (www.zinc.org).
After docking were selected 20 compounds with highest ranking for further synthesis and evaluation of biological activity.

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Pharmacophore Mapping and SAR Analysis of Na+ Channel Binding *Aconitum* And *Delphinium* Alkaloids With Diverse Biological Activity

M. A. Turabekova[a,b], Olexandr Isayev[c], Danuta Leszczynska[a,b]

[a]*Interdisciplinary Center for Nanotoxicity, Department of Chemistry and Biochemistry*

[b]*Department of Civil and Environmental Engineering, Jackson State University, 1400 J. R. Lynch Street, Jackson, Mississippi, 39217, USA*

[c]*Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106*

There is a continuous need for new, safer, more tolerable and efficacious therapeutics to treat disorders related to distracted activity of voltage-gated sodium ion channels. In fact, a slight alteration of Na+ channel gating can easily have detrimental consequences in membrane excitability that makes these channels to serve as the primary targets for a variety of naturally occurring neurotoxins and a number of therapeutic drugs. Neurotoxins that target voltage-gated Na+ channels fall into several distinct classes determined by the related receptor site they are acting at. Having taken into account that Na+ channels are diversely expressed in skeletal and cardiac muscles, central and peripheral nervous systems, the revealed structural peculiarities of binding class of compounds will aid in design of drugs selectively targeting specified type of sodium channel subtypes.

Relatively to the exerted action on the channel (opening or blocking it) these alkaloids can be considered as either neurotoxins or therapeutic agents. In this study, we have selected *Aconitum* and *Delphinium* alkaloids with arrhythmogenic, antiarrhythmic, local anesthetic and analgesic activity and that are known to bind at site #2 of Na+ channel. Five point pharmacophore models were generated separately for the each group of alkaloids to identify pharmacophore groups responsible for a particular type of activity. The predictive power of each pharmacophore was evaluated by generating 3D-QSAR model. The pharmacophore hypothesis and alignment were carried out applying Phase module of Maestro (Schrodinger, LLC, New York, 2010). PLS regression analysis was used to build QSAR models. Additionally, developed pharmacophores were docked into the KcsA-based homology model of the closed sodium ion channel applying Glide module implemented within Maestro suite. The pharmacophore models and their binding modes are discussed with respect to their exhibited therapeutic action.

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Revisiting the Diels-Alder reaction: origin of selectivity and stability of *endo*- adducts

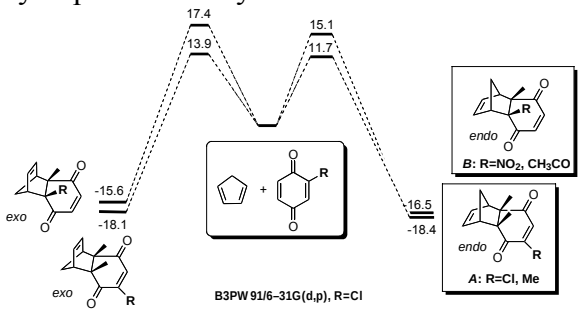
Igor A. Levandovskiy[a], Alexander Savatieiev[a], Tatyana E. Shubina[b]

[a]*National Technical University of Ukraine, Dept. of Organic Chemistry, Pr. Pobedy 37, 03056 Kiev, Ukraine; e-mail: laba123@bigmir.net*

[b]*Computer-Chemie-Centrum and Interdisciplinary Center for Molecular Materials, FAU Erlangen, Naegelsbachstr 25, 91052, Erlangen, Germany; e-mail: tatyana.shubina@chemie.uni-erlangen.de*

The Diels-Alder (DA) reaction is one of the most interesting and useful reactions found in organic chemistry. Despite the fact that it was discovered more than 80 years ago there is still no full understanding of the reaction mechanism. There are many suggestions, which attempt to explain *endo*- selectivity in Diels-Alder reaction, but none of them are firmly established. As examples, arguments such as Secondary Orbital Interaction (SOI), difference in primary overlap, difference in volumes of activation, the polarity of the transition states and release of strain energy have been used.

The DA reaction between cyclopentadiene and *p*-benzoquinone was first described in 1906 and results in the *endo*- adduct. In the case of substituted quinones, reaction with either substituted or unsubstituted double bond is possible. For example, 2-Methylquinone and 2-Chloroquinone [1] was reported to give adduct that results from reaction with unsubstituted double bond (***A*** adduct). 2-nitroquinone, 2-acetylquinone, 2-carbometoxyquinone react with cyclopentadiene by substituted double bond leading to the ***B*** adduct.



C–C bond in *exo* TS, Å		C–C bond in *endo* TS, Å	$\Delta E_{act(endo-exo)}$
2.153	PM3	2.152	0.29
2.123	AM1	2.115	0.99
2.227	HF/STO-3G	2.215	-2.05
2.261	B3PW91/6-31G*	2.243	-1.93
2.238	B3PW91/6-311+G(d,p)	2.218	-2.24
2.229	B3PW91/6-311+G(3df,2p)	2.209	-2.16
2.249	B3PW91/cc-pVDZ	2.233	-1.94
2.228	B3PW91/cc-pVTZ	2.208	-2.02
2.228	B3PW91/cc-pVQZ	2.207	-2.06
2.251	B3PW91/aug-cc-pVDZ	2.232	-2.19
2.272	MP2/6-31G*	2.262	-3.11
2.283	MP2/6-311+G(d,p)	2.272	-3.85
2.285	MP2/6-311+G(3df,2p)	2.275	-3.79

Fig. 1. Energy diagram of Diels–Alder reaction of cyclopentadiene with 2-chloro-1,4-quinone [energies are given in kcal/mol, B3PW91/6-31G(d,p)] and key parameters of the *endo/exo*-transition states at different levels of theory.

Our initial B3PW91/6–31G(d,p) calculations[1] suggest that the Diels-Alder reaction of 2-chloro-1,4-quinone with cyclopentadiene proceeds as an *inverse* Diels-Alder reaction. The formation of ***A***-type adduct is more favourable (both kinetically and thermodynamically) over the ***B***-type adduct. The lowest activation barrier is found to be 11.7 kcal/mol and corresponding transition state describes formation of the *endo*-***A***-type adduct.

Here we present results of our calculations (DFT, MP2, CASSCF) of DA reaction with 1,4-paraquinones with various substituents at 2 position and 1,4-paraquinones with various 5-substituted fulvenes. We note the absence of SOI and rather strong dependence of activation barriers and exothermicity of the reaction on basis set and level of theory. Additionally, selectivity of the DA reaction depends on polarity of the solvent.

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Circular molecular models for QSAR tasks

A.V. Liahovskiy, V.E. Kuz'min, A.G. Artemenko

A.V.Bogatsky Physico-Chemical Institute of the National Academy of Sciences of Ukraine, 86 Lustdorfskaya doroga, Odessa 65080, Ukraine; e-mail: 1dqsar@rambler.ru

In the present time QSAR analysis is important part of development of new compounds with complex of desired properties. Used QSAR methods differ from each other with way of generation of descriptors, levels of detailing of molecular structure and the algorithms of the mathematical description.

The purpose of this work is elaboration of the new method of generation of descriptors based on the circular description of molecular structure. Earlier the method based on using of structural parameters with characteristics received from the harmonic analysis of torsions angles have been offered for the description and estimations of structural similarity of cyclic structures [1].

For distribution of the similar approach on any structures the algorithm of the unified description of non-cyclic structures using parameters of pseudo-cycle is offered.

For this purpose the structure is represented as a molecular graph. For the molecular graph we solve traveling salesman problem by branch and bounds method [2]. Investigated molecular graph is represented by matrix of costs (the minimal distances between graph vertexes). As a result of the problem decision we received a pseudo-cycle that represents an initial sequence of atoms' numbers of the investigated molecule. Calculation of physical and chemical characteristics of atoms along a pseudo-cycle gives molecular spectrum. Harmonic analysis (Fourier-transform) of this molecular spectrum gives parameters for QSAR analysis.

For the estimation of efficiency of the developed QSAR approach the ability to angiotensin converting enzyme (ACE) inhibition (pIC_{50}) has been investigated [3]. Training set consists of 76 compounds and 38 structures were used in a test set. It is necessary to note that all investigated compounds are structurally homogeneous that facilitates the procedure of molecules superposition in lattice methods.

We have compare in the given work the resulting PLS-models [4] built with the use of descriptors generated in the followings QSAR approaches:

a) CoMFA – Comparative Molecular Fields Analysis; b) CoMSIA – Comparative Molecular Similarity Indexes Analysis; c) EVA – Eigenvalue Analysis; d) HQSAR – Hologram QSAR; e) Cerius 2 program package – method of traditional integral (whole-molecule) 2D и 2.5D descriptors generation;.

The advantage of the developed by us method over others has been revealed by the comparison of such statistical descriptions of QSAR models as determination coefficient for training (R^2) and test (R^2_{test}) sets; determination coefficient calculated in the cross-validation terms (Q^2); as well as the standard errors of prediction for both sets. For example for Circular model Q^2= 0.9-0.95, and for the other methods Q^2 = 0.61-0.76. Moreover, Circular models allowing determining structural fragments with positive or negative influence on investigated property as well as the contribution of different physical-chemical factors in the activity changes.

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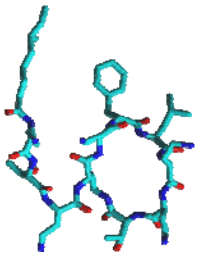
Drug-target interactions of polymyxins: A computational structure-toxicity study

Yu.V. Lisnyak[a], A.V. Martynov[a], M. Alhussein[a] and A.V. Prikolotin[b]

[a] GI "I.Mechnikov Institute of Microbiology and Immunology", National Academy of Medical Sciences of Ukraine, 14 Pushkinska str., Kharkiv 61057, Ukraine; e-mail: yulisnyak@gmail.com

[b] B.Verkin Institute for Low Temperature Physics and Engineering, National Academy of Sciences of Ukraine, 47 Lenin ave., Kharkov 61103; e-mail: Prikolotin@ilt.kharkov.ua

Polymyxin B (PMB), cyclic cationic lipodecapeptide (**1**), is highly bactericidal to multigrug-resistant Gram-negative bacteria. But therapeutic applications of this antibiotic are limited by its nephrotoxic effect which is considered to be finally due to interaction of polymyxin with megalin [1]. Megalin, transmembrane glycoprotein, contains several cysteine-rich ligand binding repeats (LBR) which share common conserved structural motifs responsible for binding of basic ligands [2] (**2**, sticks represent amino acids residues in acidic pocket of binding sites). The understanding of molecular bases of toxic effects of polymyxins can significantly assist in design of polymyxin drugs with enhanced therapeutic effectiveness.



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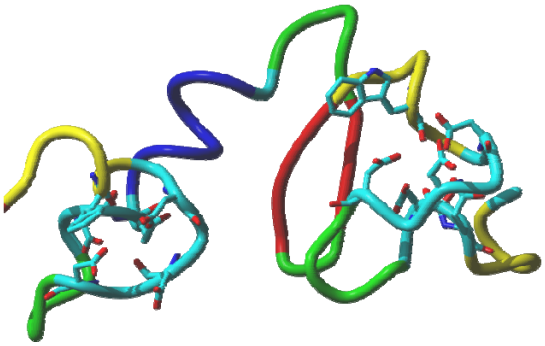

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Recently, there were synthesized novel PMB derivatives possessing significantly lower toxicity and equal activity against P.aeruginosa compared to PMB [3]. To explore structure-toxicity relationships of these compounds we carried out comparative study of peculiarities of 3D structure of PMB and its derivatives and their interactions with LBR modules of megalin by means of molecular dynamics and docking. Coordinates of starting structures were taken from [3] for PMB and from Protein Data Bank for LBR modules. Structures of PMB derivatives were built by corresponding modifications of PMB.

Our analysis revealed some key features of the interactions of PMB derivatives with LBR modules of megalin (including hydrogen bonding, mutual complementarity of electrostatic potentials as well as corresponding hydrophobic interactions within the binding sites). The possibilities of polymyxin structure optimization are discussed.

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Quantum-chemical study of fluorescent systems capable to nanoagregation

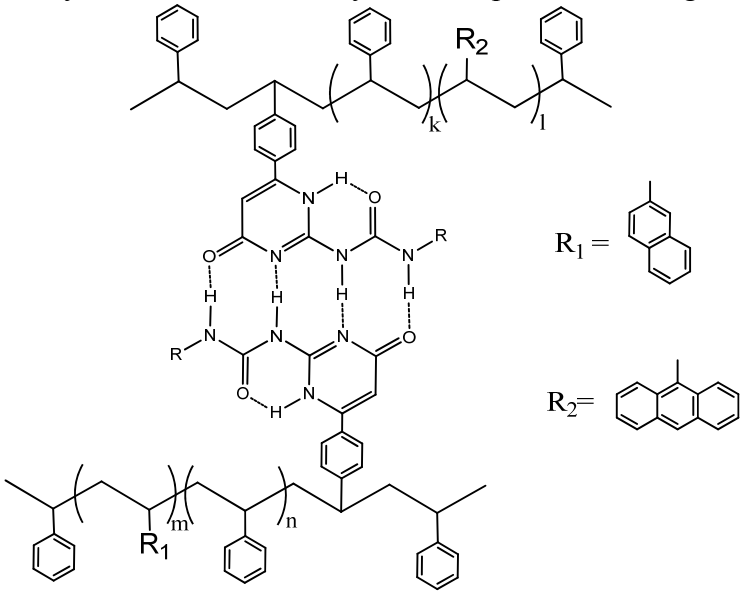
Mantel[a] A.I., Barashkov[b] N.N., Irgibaeva[a] I.S.

[a]*L.N. Gumilyov Eurasian National University, 5 Munaytpassov str., Astana, 010008, Kazakhstan*

[b]*Micro Tracers inc., Van Dyke av. 1370, San Francisco, CA, 94124, USA*

Great attention of chemists and physicists is devoted to the creation of effective fluorescent materials, which find wide application in science and technology. In this paper we paid attention to the study of polymeric fluorescent molecules which are interesting from the perspective of potential scintillation materials. By means of quantum chemistry methods were studied spatial structure and luminescent behavior of polymer systems, whose main chain is represented by a copolymer of styrene containing 2-vinylnaphtalene and 9-vinyl anthracene as comonomer units. The peculiarity of these systems is the aggregation ability in dilute solutions, owing to which it is possible to achieve the size of the obtained aggregates within hundred nanometers. The basis of the aggregation ability is formed by such compounds as 2-ureydo-4 [1H] - pyrimidinone (Upy), which has been deeply investigated in a number of works by Professor Mayer and his colleagues. A polymer chain Upy-fragment can form a quadruple hydrogen bonding with the same fragment of a neighboring polymer chain, thus leading to their cross-linking [1,2].

The study of such systems is carried out by the example of following models:



The effect of the fluorescent comonomers' concentration, their location and remoteness from each other on the luminescent properties of the system are considered.

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QTAIM analysis of hydrogen bonds in $[R_4N^+BF_4^-]$ ion pairs

Bogdan A. Marekha, Oleg N. Kalugin

V. N. Karazin Kharkiv National University, 4 Svoboda sq., Kharkiv 61022, Ukraine; e-mail: bogdan.a.marekha@gmail.com

Concentrated solutions of tetraalkylammonium (TAA, R_4N^+) tetrafluoroborates in polar aprotic solvents are widely used as electrolytic components in various electrochemical devices, especially in electric double-layer capacitors (supercapacitors).

Practically important macroscopic properties of electrolyte solutions, such as conductivity, viscosity, *etc*, are mainly determined by the microscopic structure of ionic subsystem. It is thus very important to understand the microscopic structure of the above mentioned ion-molecular systems in order to predict their behavior under various operating conditions. Apart from 'free ions', ion pairs are the major species in these systems at high electrolyte concentration, so investigation of their inner structure is of great importance. Recently the penetrated nature of ion pairs of Et_4NBr, Et_4NBF_4, Bu_4NBr, and Bu_4NBF_4 in acetonitrile was established in our laboratory [1].

The aim of the present work is to elucidate the details of inter-atomic interactions in Et_3(*n*-Pr)NBF_4, Et_4NBF_4, and Et_3MeNBF_4 ion pairs by means of quantum-chemical calculations and Bader's quantum theory of "atoms in molecules" (QTAIM) [2].

First, the structure optimization of the ion pairs mentioned above was performed at the M06-2X/AUG-cc-pVDZ level of theory. Then, for the most stable configurations (with lowest energy) of the corresponding ion pairs the electron charge density was analyzed in terms of Bader's theory "atoms in molecules". Particular attention was paid to formation of hydrogen bonds between fluorine atoms of the BF_4^- anion and hydrogen atoms of the TAA cation, Fig. 1.

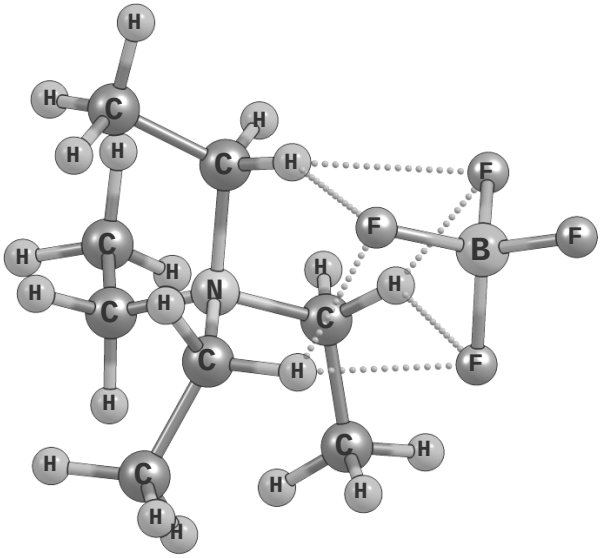

Fig. 1. One of the stable configurations of the $[Et_4N^+BF_4^-]$ ion pair. Weak bifurcated hydrogen bonds C-H···F are shown by dashed lines.

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Quantum-chemical calculations of the complex of 2,3-dichloro-1,4-naphthoquinone with triethylamine

N. Marintsova[a], M. Kurka[a], R. Zubatyuk[b], O. Shishkin[b], V. Novikov[a]

[a] National University "Lviv Polytechnic", Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, 12 S. Bandera Str., Lviv, 79013, Ukraine; e-mail: vnovikov@polynet.lviv.ua, vladnovikov@list.ru, vladnovikov@ukr.net

[b] STC "Institute for Single Crystals" of NAS of Ukraine, 60 Lenina ave., Kharkiv, 61001, Ukraine

Molecular geometry of complex 2,3-dichloro-1,4-naphthoquinone with triethylamine and its components was optimized using density functional method with dispersion correction B3LYP-D using a basic set of def2-TZVP. To achieve the minimum control, and to calculate the Gibbs free energy was calculated matrix of second derivatives of energy by atomic coordinates that did not have negative eigenvalues. Thermodynamic corrections to the energies were calculated in harmonic approximation rigid rotor at 298 K. To check the correctness of the obtained complex structure of its geometry was also optimized by unempirical method RI-MP2/def2-TZVP, which showed almost the same building complex.

The energy of interaction between the components of the complex was calculated by taking into account the errors RI-MP2/def2-TZVP superposition of basis sets by counterbalances method. Electronic absorption spectra were calculated by B3LYP/def2-TZVP metod in approximation of TD-DFT. Charges on atoms were calculated by the NBO method. In all calculations the influence of environment modeled using the COSMO continuous model, where chloroform was used as a solvent. Quantum-chemical calculations were carried out using the program package ORCA 2.8.0.

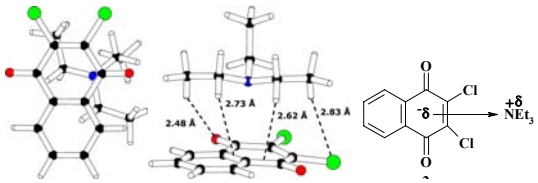


Fig.1. Structure of complex of 2,3-dichloro-1,4-naphthoquinone with trietylamine using data of MP2/def2-TZVP method

Optimization of complex geometry using MP2/def2-TZVP led to the structure (Fig. 1), characterized by the fact that the nitrogen atom of amine is located on the most electrophilic carbon atom bound with oxygen. Distance from nitrogen to the median surface of quinonic ring is 2.84 Å and the carbon atom - 2.86 Å (sum of Van der Waals radiuses are 3.21 Å), which indicates that the strong interaction between the components of the complex. At the same time contribute to the binding of the complex make weak hydrogen bonds with hydrogen atoms of etyl groups of amine. Strong interaction between the components of the complex results in markedly nonplanar structure of quinonic cycle with endocyclic torsion angles up to 8°. The possibility of such a relaxation of quinonic cycle due to its large conformational flexibility.

Calculated by MP2/def2-TZVP method interaction energy component of the complex in solution is quite large – -11.1 kcal/mol, and the complex formation energy (including energy components of complex deformation) – -7.9 kcal/mol. This Gibbs free energy of formation of the complex is +7.7 kcal/mol, indicating a very limited time of existence of such a complex in solution. Donor-acceptor complex character confirmed by analysis of the charges on components of the complex. According to the calculated total charges in the formation of the complex there is transfer of electron density from the amine to quinone – 0.1e. Despite the small number of transferred electron density, it has a significant influence on the electronic structure of the quinone, which is reflected in the calculated electronic absorption spectra of complex (Fig. 1).

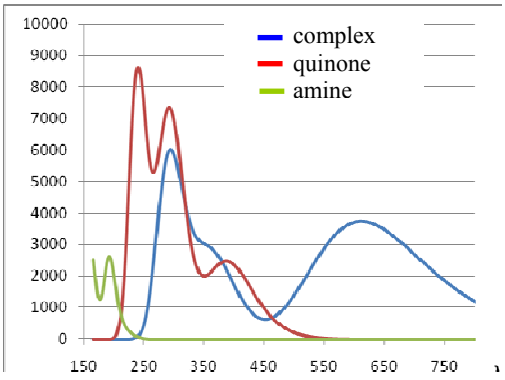


Fig. 2. Calculated electronic absorption spectrum of complex and derivatives of amine and quinone

Compared with the initial quinone, which is in the electronic absorption spectra of two close peaks in the 250-300 nm absorption spectrum of the complex appears a maximum in the 600 nm (Fig. 2).

Analysis of the molecular orbitals of the complex shows that this maximum corresponds to an electronic transition HOMO→LUMO, which is the n→π * transition with unshared electron pair of nitrogen to the vacant π-orbital of quinone.

Thus, the calculated spectra of the complex agree well with those obtained experimentally, which gives undeniable proof of donor-acceptor complex nature, which are formed by the interaction of 2,3-dichloro-1,4-naphthoquinone with triethylamine.

Complex pattern formation in simple autocatalytic models with anomalous diffusion

V. Meleshko[a], B. Datsko[a], O. Karpenko[b], C. Nakonechna[b], M. Prystay[b]

[a]*Institute of Applied Problems of Mechanics and Mathematics of National Academy of Sciences*

[b]*Institute of Physical Organic Chemistry and Cole Chemistry of National Academy of Sciences*

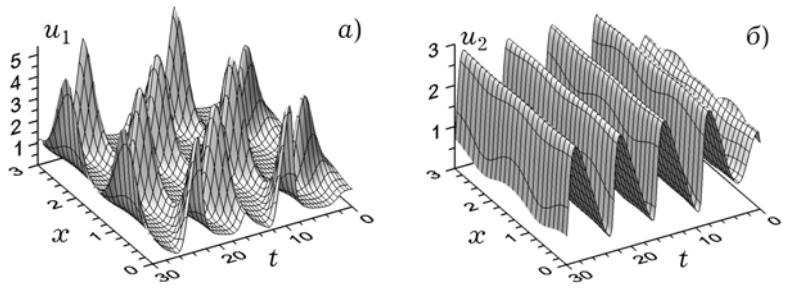
Mathematical models with anomalous diffusion are already widely used for description of processes in granular and porous media, in living tissue and different complex chemical systems. Most famous in chemistry is autocatalytic Belousov–Zhabotinsky reaction, which can demonstrate different complex autowaves of concentration of reactants in space and time. Recent it was shown that a photosensitive Belousov–Zhabotinsky system in water-in-oil microemulsion can store spatial information, even without replenishment of reactants. These new properties of Reaction–Diffusion (RD)in micro-emulsions systems can be utilized for functional memory devices [1]. In the same time nonequalibrium properties in microemulsions posses anomalous diffusion and needs a description by fractional derivatives [22]. Moreover, autowave phenomena in such complex systems are experimentally revealed, as cells and living tissues [41] give us additional reason for development and investigation of new mathematical models on the fractional RD system, which take into account anomalous nature of diffusion in such complex media. A fractional reaction-diffusion equation is derived from a continuous time random walk model and the clear difference between the patterning in different fractional reaction–subdiffusion equations provides a way of distinguishing which model might apply in a given experimental situation.

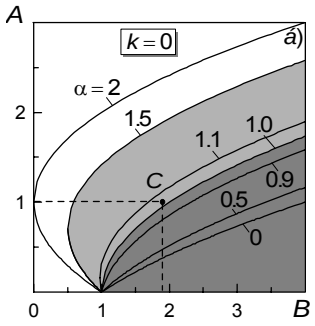
We have performed the stability analysis and computer simulation of the different autowave phenomena in fractional RD systems, based on Brusselator nonlinearities

$$\tau_1 \frac{\partial^{\alpha_1} u_1(x,t)}{\partial t^{\alpha_1}} = l^2 \frac{\partial^2 u_1(x,t)}{\partial x^2} + A - (B+1)u_1 + u_1^2 u_2, \qquad \tau_2 \frac{\partial^{\alpha_2} u_2(x,t)}{\partial t^{\alpha_2}} = L^2 \frac{\partial^2 u_2(x,t)}{\partial x^2} + Bu_1 - u_1^2 u_2 \qquad (1)$$

Here $u_1(x,t)$, $u_2(x,t)$ are the activator and inhibitor variables, $0 \le x \le l_x$, l, L are the characteristic lengths of the system, A, B - external parameters. Time derivatives on the left hand side of equations (1) instead of standard ones are the Caputo fractional derivatives. Such model describes three- molecular autocatalytic chemical reaction and represents a basis model for investigation selforganization phenomena in chemical system with anomalous diffusion.

In this work we present the possible instabilities in system (1), as well as the patterns obtained as a result of computer simulation. The obtained solutions have the form of homogeneous oscillations or inhomogeneous structures which can be stationary or oscillatory. Examples of complex pattern formation for $u1$ – (a) and $u2$ – (b) at $A = 1; B = 1{,}8; l1 = 0{,}01; l2 = 1; \alpha_1 = \alpha_2 = 1.25$ and instability domains for different degrees of anomalous diffusion presented on pictures.





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Ab initio study of electronic properties of the IO and IO^- species

Boris F. Minaev[a] and Elena M. Khomenko[b]

[a] ***Cherkassy National University, bulv. Shevchenko, 81, Cherkassy, 18031, Ukraine; e-mail: bfmin@rambler.ru***

[b] ***Cherkassy State Technological University, bulv. Shevchenko, 460, Cherkassy, 18006, Ukraine; e-mail: homenko@uch.net***

Halogen-containing species, such as monoxides of the halogens, XO (X=Cl, Br, I) are especially important for the ozone catalytic depletion cycle in the lower atmosphere. Calculations of the fine and hyper-fine structure parameters of the IO radical are important in connection with the optical monitoring of the lower atmosphere. Thus the detailed studies of the fine structure of IO and IO^- species since all these properties are strongly influenced by relativistic effects. In the previous papers an electronic structure in ratio-frequency, microwave and UV-visible region of the IO, IO^- and HOI species have been calculated by ab initio methods with account of relativistic effects [1]. Also we have early predicted that all XO^- anions have predissociative character and are metastable in the low-lying excited vibrational levels because of spin-orbit coupling integral between the ground $X^1\Sigma^+$ and the lowest excited $^3\Pi$ triplet states at the crossing points is nonzero [2].

We will present our results of multi-configurational self-consistent field (MCSCF) calculations with the Sadlej basis set for a large variety of observable electrical, magnetic, rovibronic and structural properties in order to make well-grounded interpretations of the spectra of the IO^- and IO molecules. The predicted rotational and vibrational spectra and other magnetic properties are in good agreed with experimental data. The results of the properties calculations for the IO radical and IO^- anion are presented in the table.

Table – MCSCF (Sadlej basis) calculated electronic properties of the IO radical and IO^- anion at optimized geometry for the ground and few excited states

State	R_e	ν_e	$e^2q_{zz}Q_I$	$e^2q_{zz}Q_O$	μ	α_{xx}	α_{zz}	g_r	NSRC	χ_{iso}
IO										
$X^2\Pi$	1,906	653 (8,12)	-1928,1	14,39	2,14	32,75	51,53	-0,159	-60,51	71,61
experiment	1,87	686	-1907	-	2,3	-	-	-	-	-
$a^4\Sigma^-$	4,483	43,2 (0)	1158,4	-10,32	0,03	35,58	38,32	-0,062	-	-48,91
IO^-										
$X^1\Sigma^+$	1,954	587 (0,14)	-1791,2	-15,79	4,21	51,54	66,06	-0,143	-47,48	-11,2
experiment	1,929	581	-	-	-	-	-	-	-	-

R_e is the equilibrium I-O distance in Å; ν_e is the vibrational frequency in cm^{-1}; IR transition intensities (km/mol) are given in parentheses; $e^2q_{zz}Q_I$ is the iodine nuclear quadrupole coupling constant in MHz; $e^2q_{zz}Q_O$ is the oxygen nuclear quadrupole coupling constant in MHz; μ is the dipole moment in Debye; $\alpha_{xx}=\alpha_{yy}$ are the perpendicular components of the static polarizability in a_0^3; g_r is the rotational g factor in a.u.; *NSRC* is a spin-rotation coupling constant for ^{127}I nucleus in kHz; χ_{iso} is isotropic diamagnetic (temperature independent) susceptibility in a.u.

The calculated nuclear quadrupole coupling (NQC) constant of the ^{127}I isotope in the ground state of the IO radical (-1928,1 MHz) at the optimized R_e distance is in excellent agreement with the experimentally obtained from the gas-phase EPR spectrum of the IO radical (-1907±13 MHz). We have predicted the NQC value constant for the ^{17}O isotope of the $I^{17}O$ radical to be equal 14,39 MHz. This constant is not known from experimental since the $I^{17}O$ isotope has not been studied so far, but, for comparison, the NQC constant for the ^{17}O isotope in the ground state of the $^{17}O^{16}O$ molecule is equal to –8,3 MHz and this NQCC has an opposite sign to that of the IO radical.

The calculated and predicted magnetic properties of IO and IO^- species can be useful for future experimental studies.

[1] B.Minaev, O.Loboda, O. Vahtras, H. Agren, E. Bilan, Spectrochimica Acta Part A 58 (2002) 1039-1053.

[2] B.Minaev, E. Khomenko, J. Struct. Chemistry 42 (2001) 587-591.

Structural analysis of Modified base pairs in RNA

Mohit Chawla and Rupali Sharma

Lovely Professional University, Punjab, India; email: mohitchawla.bt@gmail.com

Base pairs involving modified nucleotides constitute an important class of RNA base pairing systems, several of which nucleate higher order structures and participate in tertiary interactions joining distant regions in RNA structures. Here we present our attempts at understanding the roles of such base pairs by detecting all such possible modified base pairs in available non redundant dataset of RNA crystal structures using BPview program, in their specific structural contexts and by characterizing their geometries. The comprehensive analyses for the occurrence of modified base pairs is done on the non-redundant dataset of RNA crystal structures. Based on their occurrence contexts and functional features, modified nucleotides can be divided into two distinct classes, viz. Class I, where the modified residue is engaged in hydrogen bonding with partner modified/natural residue at the site of modification and class II, where the modification site is not directly involved in hydrogen bonding with partner natural/modified residue . The modified residues are observed mostly in case of t-RNA structures. The conservation and co-variation analyses is also performed where a triplet interaction 13C:22G:46g involving a modified residue is found to be conserved across different t-RNA molecules . In addition, the diversity in hydrogen bonding pattern is also observed for some of the base pairs belonging to the same geometrical class.

Estimation of ZPV corrections to NMR parameters via anharmonic calculations

Marzena Nieradka[b], Justyna Skórzewska[a], Teobald Kupka[b], Małgorzata A. Broda[b], Aneta M. Buczek[b]

[a]*Department of Biosystematics, University of Opole, Opole*

[b]*University of Opole, Faculty of Chemistry, Poland*

Theoretical calculations of NMR parameters (nuclear isotropic shieldings and indirect spin-spin coupling constants) are essential to support experiment and predict spectral parameters. The accuracy of calculated parameters depends on the inclusion of correlation effect, method of calculation, size and flexibility of the basis set, intermolecular interactions, temperature, as well as on corrections due to molecular rovibrations.

The ZPV corrections are necessary to obtain highly accurate theoretical NMR parameters. For practical reasons density theory methods and smaller basis sets are used to evaluate ZPVC.

The VPT2 method (second order vibrational perturbation theory) has been implemented by Barone in Gaussian program. It was claimed as "a fully automated technique" in a "black box" manner.

The aim of our work is to compare NMR parameters of several model molecules calculated at equilibrium and rovibrationally averaged geometry with experimental and high level theoretical results from the literature and to estimate the accuracy of calculations. The results of calculations using B3LYP hybrid density functional with selected Jensen basis sets will be discussed.

The nuclear magnetic shieldings of water calculated at equilibrium and rovibrational averaged geometry are shown in Tab.1.

Tab.1. Comparison of CBS estimated isotropic nuclear shieldings of water calculated for equilibrium and rovibrational averaged geometry.

Basis Set	Equilibrium geometry		Rovibrational averaged geometry	
	O	H	O	H
pc-n	324.8	30.8	316.5	30.3
aug-pc-n	325	30.8	316.7	30.3

[1] K. Ruud, Per-Olof Åstrand, P. R. Taylor J. Am. Chem. Soc., 2001, 123 (20), pp 4826–4833

[2] T. Kupka, M. Stachów, M. Nieradka, J. Kaminsky, T. Pluta, *J. Chem. Theory Comput.,* 6 **(2010)** 1580-1589.

[3] V. Barone, *J. Chem. Phys.* **2004**, *120*, 3059.

[4] V. Barone, *J. Chem. Phys.* **2005**, *122*, 014108.

Statistical properties of intramolecular hydrogen bonds in the DNA structural units

T. Yu. Nikolaienko[a], L. A. Bulavin[a], D. M. Hovorun[b,c]

[a] *Taras Shevchenko National University of Kyiv, Faculty of Physics, Molecular Physics Department, pr. Hlushkova 4, Kyiv 03022, Ukraine; e-mail: tim_mail@ukr.net*

[b] *Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine*

[c] *Institute of High Technologies, Taras Shevchenko National University of Kyiv*

Intramolecular hydrogen bonds (iHB) play crucial role in biological molecules functioning and in formation of their structure. In the present work we've focused on investigation of statistical properties of iHB found in numerous conformers of the following molecules: 1,2-dideoxyribose (55 conformations), 2-deoxy-D-ribofuranose (201), 2'-deoxycytidilic acid (613) [1] and 2'-deoxythymidilic acid (660) [2] molecules. In all, as many as 3773 iHBs were revealed by R.Bader's QTAIM method in 1529 structures obtained at the DFT B3LYP/6-31G(d,p) level of theory. **Figure 1** below gives an example of *X*H···O (X = C, O) type iHB geometrical properties distribution in terms of H···O distance and *XHO* angle and **Figure 2** represents statistical properties of electron density values (ρ^{cp}) in (3,-1)-type bond critical point. Linear correlations between iHBs energy and some of their geometrical and physical properties were revealed by the correlation analysis procedure.

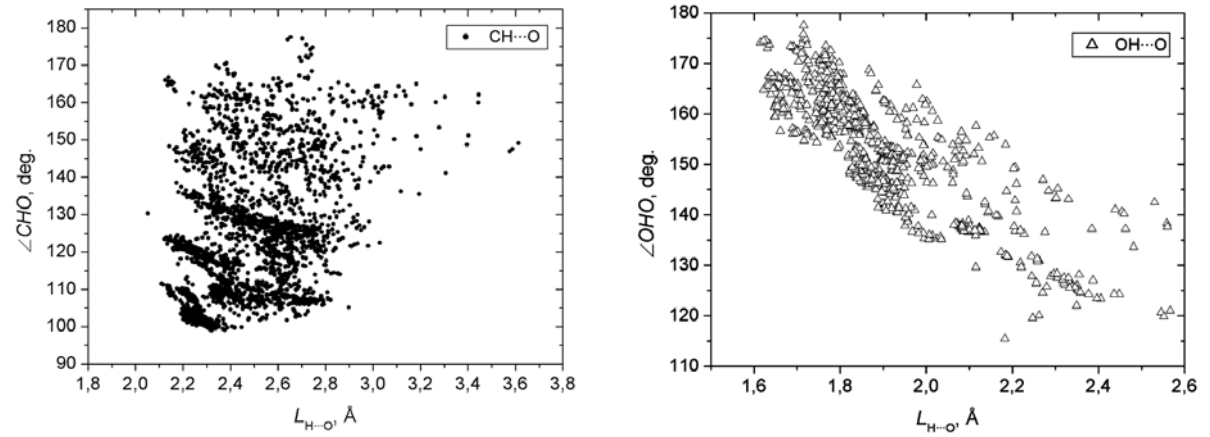


Figure 1. Geometrical properties distribution for CH···O and OH···O iHBs

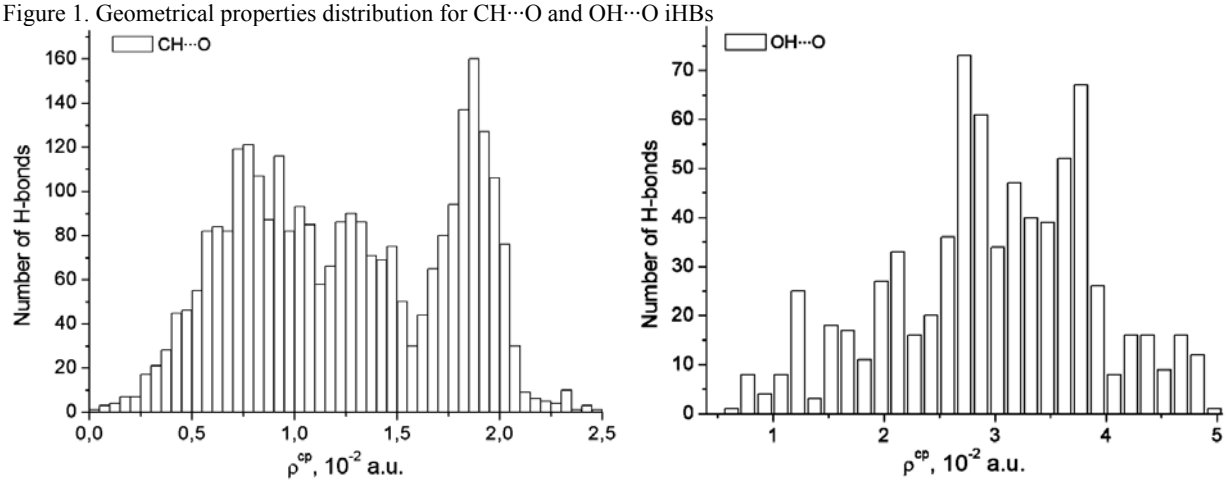


Figure 2. Bond critical point electron density values distributions for CH···O and OH···O iHBs

[1] Bulavin L.A. *et al.* Proc. Nat. Acad. Sci. Ukraine (2010), No. 10, p. 166.

[2] Nikolaienko T.Yu., Bulavin L.A., Hovorun D. M. Ukrainian Biochemical Journal (2010), *in press*

Virtual screening and computer-based assesment of potential biological activity of synthetic biocides

Vasylyuk S.V., Platonov M.O., Shved O.M., Lubenets V.I., Novikov V.P.

Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, Lviv Polytechnic National University, 12 S. Bandera Str., Lviv, 79013, Ukraine; e-mail: vnovikov@polynet.lviv.ua

Searching of molecular structures with directional biological action includes a targeted chemical synthesis, biosynthesis or extraction of substances from natural substrates, which requires the application of a new method of biological activity prediction.

Creation of modern products with high quality and reliability at an affordable technology requires providing of improved and predefined properties to materials, foodstuffs and medicines, with aim of diversification, increasing the efficiency and safety of the goods portfolio, passing examination under the modern system of production control GMP and requirements of international quality standards ISO.

Problem of creating of biologically active compounds for the obtaining of effective biocides, medicines, nutritional bioadditives, dyes, preservatives and bio resistant polymeric materials is researching at our department by holding the chemical synthesis of analogues of natural compounds of tiolsulfonate and hinoid range, and getting extractive substances, pigments and biocides with high index, wide specter of biological activity and specific physiological properties.

Biological damage of materials caused by different types of bacteria or fungi, but large groups of different microorganisms, due to this for materials protection from damage can be used substances that exhibit a wide spectrum of antimicrobial activity. In compounds with this biological activity include analogues of natural antioxidant phytonym, namely 1,4-quinone and naphthoquinone derivatives and analogues of natural allicin phytoncides S-esters of tiosulfonates which, as toxic compounds (LD50 = 2000 ÷ 2500 mg / kg) exhibit a wide spectrum antimicrobial activity, high anti-bacterial and fungicidal activity and is recommended as preservatives to protect against disease in long-term phyto storage, as proposed for the synthesis of Various synthones on the basis of new biologically active dyes and biocides, as well as to develop an effective antimicrobial drugs.

Perspective is the use of replacements for the synthesis of natural pigments, as the use of flavonoids, which include anthocyans for coloring foods now limited extracts strongly pigmented fruits and preparations anthocyans currently not used, because at pH above 4 their coloring is unstable. However, methods for stabilizing these compounds in the pH range typical for this food and beverages are developing.

Today, scientists of department had synthesized about a thousand and hinoid and tiolsulfonate synthetic derivatives of antimicrobial action, but their number has exceeded the ability of comprehensive, study and analysis of their biological effects through rapid testing for bacterial and fungal series of museum strains of crops and determine the toxicity of using available experimental studies on animals, analysis of information on substances bioactivity analogues at different levels of living matter, and interpolation of data obtained. Therefore interesting for us is a new scientific direction - Bioinformatics, which focuses on the study of biological objects by methods of mathematics and computer science.

The relationship between molecular structure and biological activity is a fundamental characteristic of activity of biologically active compounds, as well as the structure depends on a set of parameters providing the ability to penetrate substances into the cell and reach the contact, avoiding inactivation of components of cells, counteracting the destructive enzymes, interacting with active receptors That determines the degree and direction of biological effect.

One promising and rational direction of bio activity forecasting is the application of screening methods for bioactive compounds by analyzing the relationship "structure-activity" by using computer technology (in particular known method of modeling the relationship of "C-A" (method of group argument). Calculated experiment on the principle of computer models, according to which the review is focusing on constantly complicated structure models and their selection and evaluation according to certain criteria. Application of authentic parameters of bio activity of models are based on preliminary data obtained by express biotesting, determination of physical and chemical properties, molecular weight values etc.

We use well known programs and models to predict the properties of natural and synthetic chemical structures and correction of experimental data and validation of prognostic data with biological activity required by the molecular structures of the synthesized compounds for obtaining potential biological and tiolsulfonate hinoid compounds.

Comparison of properties of synthesized thio compounds and polymers on the basis of calculated data of predicted bio activity a low toxicity will provide an opportunity to offer new substance to fill the portfolio of effective biocidal drugs.

Bioinformatics easily merged in pharmacology. Bioinformatics methods allow to reach a new level in solving fundamental problems in deciphering of biological ultrastructure, being complex biomolecular systems in designing drugs and biotech products. Using computer forecasting can reduce the term of design preparation from 5-6 years to months. Therefore, we believe that the use complex methods of modeling self-models not only provide a prediction of properties of potential biocides, but also suitable for studying index of bio activity known compounds and bioadditives, as well as open the possibility of increasing efficiency and expanding the coverage of previously synthesized but not evaluated for bio activity compounds.

For the synthesized tiolsulfonate was made virtual screening of biological activity using the computer program PASS, which predicts structural formula for the chemical of 565 species of biological activity, including main and side pharmacological effects, mechanisms of action, mutagenicity, carcinogenicity, and teratohenicity, embrio toxicity (average prediction accuracy in sliding control is about 85%, which is sufficient for its application in practice to forecast range of biological activity of new compounds - the expected average prediction accuracy of random guessing one of the 500 species of activity is only about 0,2%).

Obtained results indicate prediction of biological activity on the feasibility of experimental of biological research. Based on the screening of biological activity of the was carried out by a computer program PASS shows the priorities of experimental studies of these substances. In particular, is appropriate to study their antineoplastic, antidiabetic, antiviral, pain, antiasthmatic, antibacterial, antifungal, antihelmintic and antialcoholic effects. Also the influence of thiosulfoester on fertility enhancer, central nervous system and heart failure treatment should be studied.

Results of preliminary biological screening of predicted activity of the selected thiosulfosubstances using the program PASS, QSAR and primary microbiological experimental studies for the creation of appropriate drugs show feasibility to make research in this area, and the need for expansion of existing databases and creating of new databases in order to fill the commercial portfolio.

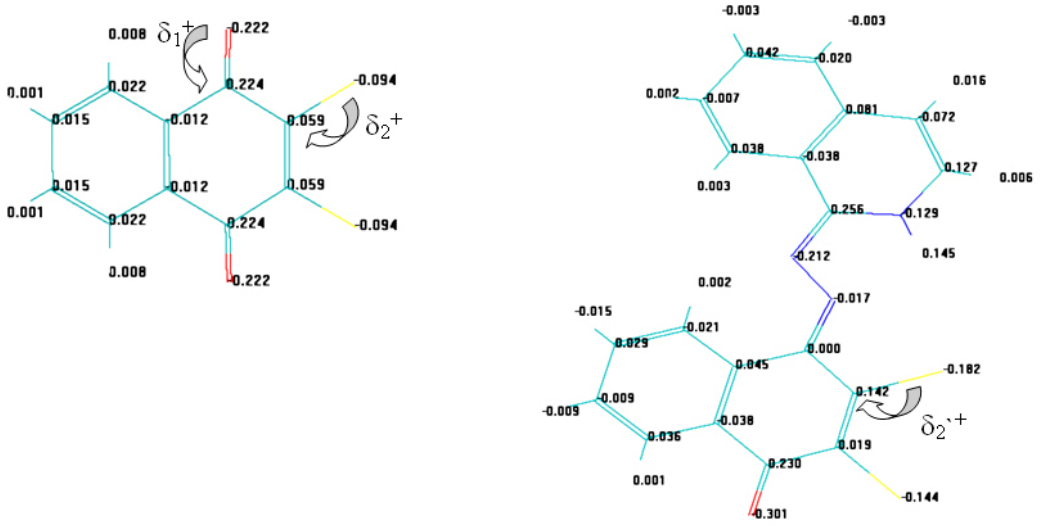
Computer modeling and synthesis of quinazoline derivatives of 1,4-naphtoquinone

A. Karkhut, Ch. Bolibrukh, O. Kovalchuk, V. Ogurok, A. Kudrinetska, V. Syngaevsky, S. Polovkovych, V. Novikov

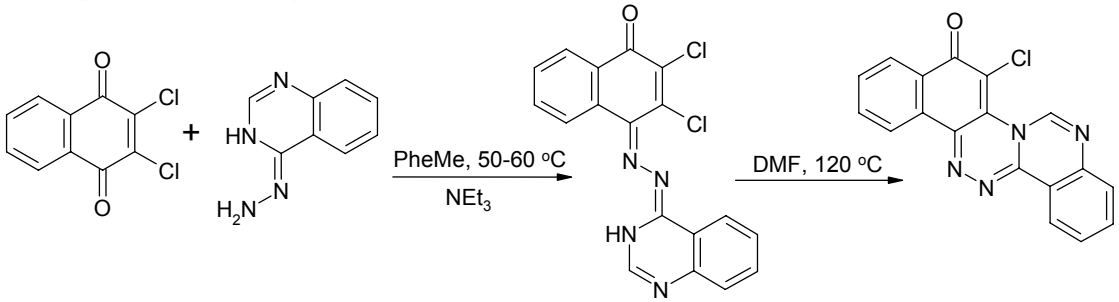
National University "Lviv Polytechnic", Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, 12 S. Bandera Str., Lviv, 79013, Ukraine; e-mail: vnovikov@polynet.lviv.ua, vladnovikov@list.ru, vladnovikov@ukr.net

2,3-dichloro-1,4-naphthoquinone is a promising reagent for the synthesis of multifunctional compounds, as it contains several active centers. Depending on the conditions of synthesis interaction of 2,3-dichloro-1,4-naphthoquinone with N,N-binucleophiles can proceed on the alternative ways.

Using the computer modeling program HyperChem a calculation of the location of charges in the molecule of 2,3-dichloro-1,4-naphthoquinone was carried out, that showed rather large positive charge on the atom of carbon in 1 and 4 positions. Therefore, in the interaction with the studied hidrazines will be formed corresponding azomethines as the products. While carrying out quantum-chemical calculations of obtained azomethines was found that using as substituent hydrazide quinazoline, the charge distribution is such that positive charge at a nearby with azomethine group atom of carbon increases.



So, we can confirm about the possibility of nucleophilic attack of the C^3-atom of carbon by nucleophilic center of quinazoline nucleus.



Experimentally this interaction was conducted in the harsh conditions and 8-chloro-9*H* naphtho[2',1':5,6][1,2,4]triazino[4,3-*c*]quinazolin-9-one was obtained.

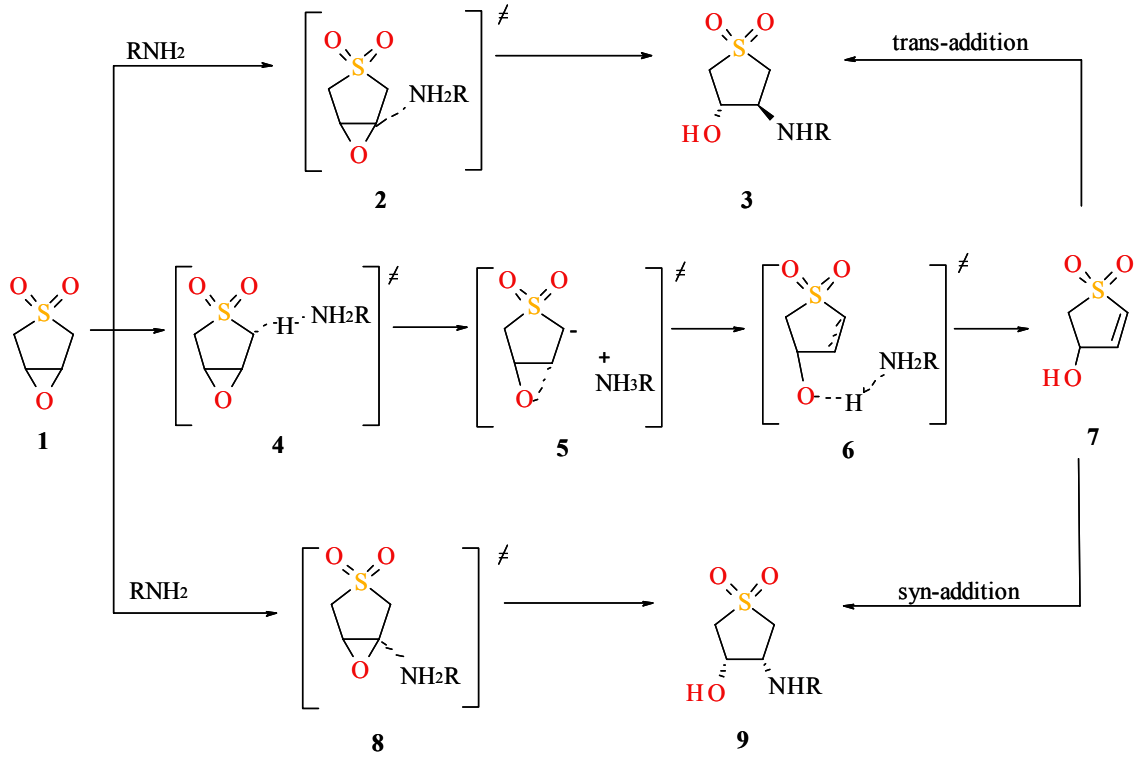
Theoretical investigation of aminolysis reaction of 3,4-epoxysylfolane

Okovytyy S., Borisenko I., Kovalchuk M.

Dnepropetrovsk National University named after Oles Honchar, e-mail: sokovyty@icnanotox.org

The 3,4-epoxysylfolane derivatives have attracted considerable attention due to their high reactivity towards a wide range of reagents: alcohols, tioalcohols, acids and other reagents and wide range of biological activities.

In the present study the mechanisms of reaction of 3,4-epoxysylfolane (**1**) with ammonia and hydrazine have been investigated. Calculations have been performed at the B3LYP/6-31+G(d), M062X/6-311++G**, MP2/6-311++G** levels of theory in the presence of water as solvent both with explicit consideration and using Polarizable Continuum Model. All possible reaction pathways were discussed.



R=H, NH_2

The obtained results show that the formation of trans- (**3**) and syn-aminoalcohol (**9**) can pass through one-step trans- and syn-openning of epoxy cycle respectively or through allylic rearrangement.

The allylic rearrangement occurs in several steps: 1) proton transfer from carbon atom of amine molecule, 2) proton transfer from the amine molecule to the oxygen atom of expoxy ring, 3) formation of double C = C bond; and, finally, 4) ammonia (hydrazine) addition to double bond with formation trans- and syn-products of 3,4-epoxysylfolane aminolysis.

The interaction of dipropylamine with carbon dioxide: an experimental study of reaction kinetics and quantum chemical calculations

M.T. Omirzak[a], I.S. Irgibaeva[b], N.N. Barashkov[c]

[a,b] *Department of Chemistry, Gumilyov Eurasian National University, Munaitpassov Str. 5, 010000, Astana, Kazakhstan*

[c] *Micro-Tracers, Inc, 1370 Van Dyke Ave, San Francisco, CA 94124, USA*

The global warming caused by increased concentration of carbon dioxide in the atmosphere, resulting from large-scale burning of fossil fuels is becoming one of the major environmental problems. In the recent research publications possibility of using ionic liquids as alternative carbon dioxide absorbents has been widely discussed.

The purpose of this study was the investigation of carbon dioxide interaction mechanism with secondary amines, forming ionic liquids by experimental and quantum-chemical methods.

The rate of CO_2 absorption in dipropylamine (99%) was measured by gravimetric method at local ambient pressure. According to the results, the increase in the rate of absorption over time was determined (Figure 1).

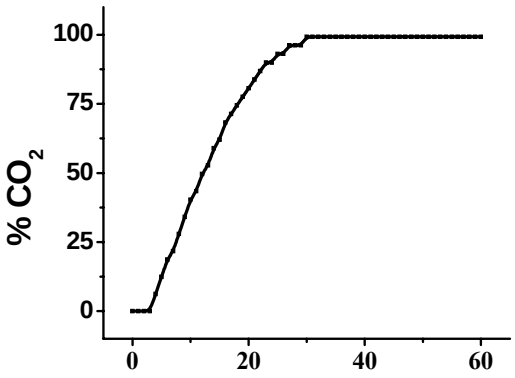


Figure 1. The rate of CO_2 absorption of dipropylamine as a function of time at 1 atm.

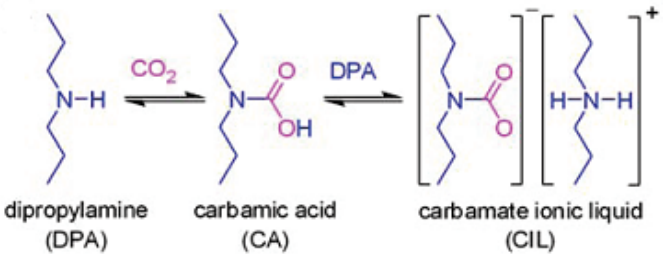


Figure 2. Reaction of DPA with CO_2 leads to the formation of CA and ionic liquid - CIL.

When interacting with CO_2 dipropylamine reversibly forms highly polar viscous ionic liquid – dipropylamine carbamate salt, which can be easily converted back to the nonionic liquid by bubbling it through an inert gas such as nitrogen or by heating to a certain temperature.

To reveal the interaction mechanism of CO_2 with dipropylamine quantum chemical calculations were performed. The calculated model of the reaction between carbon dioxide and two molecules of dipropylamine is shown in Figure 2.

Geometry optimizations of the dipropylamine (DPA) and carbon dioxide, dipropylamine carbamic acid (CA), dipropylamine carbamate ionic liquid (CIL) possible structures, their total energies calculations were carried out with the use of Becke's three-parameter hybrid method with Lee, Yang, and Parr (B3LYP) gradient-corrected correlation functional and the standard 6–31+G(d,p) basis set.

Using the optimized by DFT method geometry for the three stationary points: DPA + CO_2 + DPA, CA + DPA and CIL was found that the structure CA + DPA is a transition state in CO_2 reaction with dipropylamine.

Atom-scale Molecular Model of Dengue Virus Envelope Proteins and Membrane

Dmitry I. Osolodkin[a], Vladimir A. Palyulin[a], Nikolay S. Zefirov[a], Vladimir M. Pentkovski[b]

[a] *Department of Chemistry, Moscow State University, Moscow, 119991, Russia*

[b] *Moscow Institute of Physics and Technology, Dolgoprundny, Moscow Region, 141700, Russia*

Dengue fever is a major health concern in tropical countries, affecting millions of people worldwide. This disease is caused by dengue virus (DENV), which belongs to the genus *Flavivirus* along with tick-borne encephalitis virus, yellow fever virus, West Nile virus, Japanese encephalitis virus, etc. Flaviviruses are characterised by enveloped icosahedrical virions; viral capsid is formed by proteins E and M anchored in the lipid membrane. Viral fusion is primed by pH decrease: upon this process E proteins rearrange and form spikes that attack the host membrane and lead to the injection of viral RNA into the cell. Study of the dynamics of this conformational rearrangement is of a great importance for the design of new antiviral drugs, targeting not only DENV, but also other enveloped viruses.

We present a full atom-scale molecular model of the DENV envelope building block: the complete model of E protein dimer including transmembrane helices, accompanied by M proteins and corresponding regions of membrane. The model was constructed with the help of previously published low-resolution cryoelectron microscopy maps [1] and optimised by simulated annealing and conventional molecular dynamics procedures. The model is a reasonable starting point for large-scale molecular dynamics simulations regarding the mechanism of pH-dependent flavivirus activation.

[1] Zhang W. et al., *Nat. Struct. Biol.,* **2003,** *10,* 907-912.

Theoretical investigation of protonated forms of 2'-deoxyguanosine-5'-phosphate

Gennady V. Palamarchuk[a,b,*], Oleg V. Shishkin[a,b,c], Leonid Gorb[b,c,d], Jerzy Leszczynski[b,c]

[a] ***SSI "Institute for Single Crystals," NASU, 60 Lenina Ave., Kharkiv 61001, Ukraine; e-mail: gena@xray.isc.kharkov.com***

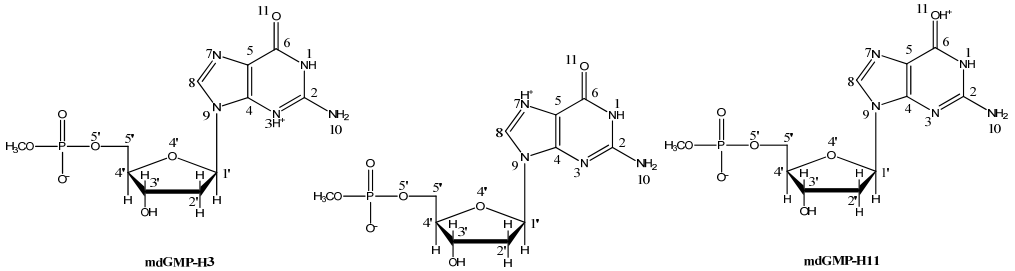
[b] ***Ukrainian-American Laboratory of Computational Chemistry, Kharkiv, Ukraine, and Jackson, Mississippi***

[c] ***Interdisciplinary Center for Nanotoxicity, Jackson State University***

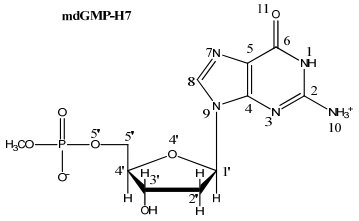
[d] ***Department of Molecular Biophysics, Institute of Molecular Biology and Genetics, NASU, 150 Zabolotnogo str., Kyiv 03143, Ukraine***

The main interest in canonical 2'-deoxyribonucleotides (DNT) is caused by the fact that they are building blocks of DNA. In addition, nucleotides can carry out functions of cofactors, allosteric effectors, part of coenzymes, directly participate in a metabolism, and also in processes of accumulation, transfer and transformation of energy. Protonation of nucleic acid bases is a well known process which is responsible for stabilization of DNA triplexes, mispairing of complementary bases, formation of complexes of transition metals with bases etc. In particular those concerns 2'-deoxyriboguanosine monophosphate.

Quantum-chemical calculations by B3LYP/aug-cc-pvdz method of tautomers of protonated methyl ether of (mdGMP) revealed existence of four isomers with proton attached to different heteroatoms namely carbonyl oxygen (mdGMP-H11), purine nitrogen atoms N3 (mdGMP-H3) and N7 (mdGMP-H7) and amino group nitrogen (mdGMP-H10). The isomer with protonated N1 atom of the base is the most stable.



mdGMP-H3 mdGMP-H11



mdGMP-H7

mdGMP-H10

Protonation of guanine moiety leads to the considerable strengthening of intramolecular C-H…O and N-H…O hydrogen bonds. This is caused by increase of electrostatic interaction between two charged fragments of molecule namely anionic phosphate group and protonated base. At the same time drastic changes of conformation of nucleotide are observed. In the case of anti-conformers of mdGMP protonation of base leads to transition to syn-conformation. All such syn-confomers are stabilized by strong intramolecular N-H…O hydrogen bond. In some cases it is observed the proton transfer from the base to phosphate group. Such process leads to the formation of tautomer without charged fragments. Besides that protonation leads to a change of conformation of ribose from north to south.

DFT Study of Solvent Effects on Conformational Equilibria and Vibrational Spectra of 4-Cyclohexylpiperidine

Gürkan Keşan [a], Cemal Parlak [a], Özgür Alver [b] and Metin Bilge [c]

[a] *Department of Physics, Dumlupınar University, 43100, Kütahya, Turkey*
[b] *Department of Physics, Anadolu University, 26470, Eskişehir, Turkey*
[c] *Department of Physics, Ege University, 35100, İzmir, Turkey*

The optimized structural parameters (bond lengths, bond and dihedral angles), conformational equilibria and vibrational spectra together with assignments of 4-cyclohexylpiperidine (4-cypp) have been examined by means of B3LYP hybrid density functional theory (DFT) method with 6-31G(d) basis set. Furthermore, reliable vibrational assignments have made on the basis of potential energy distribution (PED) calculated. Calculations are employed for different conformations of 4-cypp ($C_{11}H_{21}N$), both in gas phase and in solution. Solvent effects on the geometric parameters, vibrational frequencies, IR intensities and Raman activities of 4-cypp have been investigated using chloroform-*d* and dimethylsulfoxide-*d*. Results from the theoretical values are showed that the structural parameters, mole fractions of stable conformers, vibrational frequencies, IR intensities and Raman activities of 4-cypp are solvent dependent.

On possibility of transferring ab initio force fields by converting them to dependent coordinates set

Pitsevich G.A.

Belarusian State University, Minsk, Belarus

For the case of a planar molecular fragment with three valence angles having a common vertex and involving a single dependent coordinate the problem of reconstructing the force field in the dependent set of coordinates has been solved successfully [1]. However, as the tetrahedral fragment is most usual in polyatomic molecules, elucidation of the possibility for similar transformations in this case will contribute considerably to the applicability of the method.

We denote the dependent set of normal coordinates as $\|\mathbf{Q}\|$ and the independent set – as $\|q\|$. Both sets are related to each other by the matrix A : $\|Q\| = A\|q\|$ (1). For the regular tetrahedral fragment the matrix A well known and pseudoinverse matrix A^{-1} can be found. Denoting the matrix of force constants for the dependent set of natural coordinates by K and the corresponding matrix of the independent set – by k, we can state that for the known K one can always find the matrix k unambiguously as soon as the matrix A, expressing the dependent set of natural coordinates in terms of the independent one, is defined [2]. Proceeding from the general considerations, the matrix k must be of the form

$$k = \begin{pmatrix} 2y & x & y & y & 2y-x \\ x & 2x & x & x & x \\ y & x & 2y & 2y-x & y \\ y & x & 2y-x & 2y & y \\ 2y-x & x & y & y & 2y \end{pmatrix} \quad (2)$$

Using the transformation $K = \tilde{A}^{-1} \cdot k \cdot A^{-1}$ (3) we can derive the general form of the matrix of force constants for deformation coordinates in the dependent set as follows:

$$K = \frac{1}{6}\begin{pmatrix} 4y+x & x-2y & x-2y & x-2y & 4y-5x & x-2y \\ x-2y & 4y+x & x-2y & x-2y & x-2y & 4y-5x \\ x-2y & x-2y & 4y+x & 4y-5x & x-2y & x-2y \\ x-2y & x-2y & 4y-5x & 4y+x & x-2y & x-2y \\ 4y-5x & x-2y & x-2y & x-2y & 4y+x & x-2y \\ x-2y & 4y-5x & x-2y & x-2y & x-2y & 4y+x \end{pmatrix} \quad (4)$$

With the use of the inverse transformation $k = \tilde{A}KA$ (5) we can see that the form of the matrix k remains similar to (2). The acceptability of such transformations was checked with a molecule of methane. Based on the quantum-chemical program packages [3], for this molecule in the approximation B3LYP/cc-PVTZ a force field has been calculated in the independent set of vibrational coordinates together with a spectrum for normal vibrations. With the help of relation (5), the force field was reconstructed in the dependent set of coordinates. Then the original molecular geometry and the matrix of force constants K have been used as the starting data for the computation of normal vibrations with the package [4]. Coincidence in the frequencies calculated with the help of the packages [3] and [4] supports the applicability of the developed method to the regular tetrahedral fragment.

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Computer simulation of electron spectra of monomer and low-size clusters of methanol molecule in the approximation TD-DFT/B3LYP/cc-pVTZ

Pitsevich G.A.[a], Doroshenko I.Yu.[b], Pogorelov V.Ye.[b], Melnikova E.A.[a]

[a] *Belarusian State University, Minsk, Belarus*

[b] *Kiev National Taras Shevchenko University, Kiev, Ukraine*

The existence of the internal rotation in methanol molecule and its ability to form various cluster structures leads to the fact that in literature it is referred as the most complex among the simplest ones and the simplest among the most complex ones. The large number of works is devoted to the spectroscopic investigations of this molecule, but only few of them use electron spectroscopy [1-3]. The available theoretical works [1, 4] deal with methanol monomer. The results of these calculations are in a good agreement with the electron spectra of methanol in matrix isolation, but the corresponding spectra in the condensed phase even at low temperatures have more complex structure [3]. The calculations of molecular orbital energies, electron states and oscillator forces of methanol monomer, dimer, chain and two conformers of cyclic trimer were carried out using the quantum chemical packet [5] in the approximation TD-DFT/B3LYP/cc-pVTZ. The most long-wave absorption band in methanol spectrum (54520 cm^{-1}) is related to the transition from ground electron state $0A'$ to the first excited one $1A''$. The calculated value of the frequency of the mentioned transition is 56120 cm^{-1}, at this the transition of the electron from the highest occupied orbital $(2a'')^2$ to the lowest vacant one occurs. According to our calculations, in the highest occupied molecular orbital besides the non-bonding p_z orbital of the oxygen atom the bonding group σ orbitals of C-H bonds of a'' type are presented. The properties of the lowest vacant orbital are determined by the loosening group σ orbital of hydroxyl group, which in whole agree with the data [1]. The calculated frequencies of the next three frequencies of the transitions in the methanol molecule are 65879, 70533, 75461 cm^{-1}. The calculated electron spectra of the methanol clusters in the interval 50000-75000 cm^{-1} contain considerably larger numbers of the absorption bands in comparison with the monomer spectrum. For example, already in the calculated spectrum of dimer in the mentioned interval there are 12 absorption bands. The highest occupied molecular orbital of the dimer is fully localized at the donor molecule and in its nature is identical to the analogous orbital of monomer. The lowest vacant orbital in the dimer also maintains its nature, but it is located at the acceptor molecule. As a result, the most long-wave transition is related to the charge transfer from the donor molecule to the acceptor one. It stabilizes the dimer due to the electrostatic interaction. The increasing of the cluster size leads to the increasing of the absorption bands number and, taking into account the large half-widths of the bands, to the decreasing of the spectrum structurization, which is also observed in the UV spectra of pure methanol [3].

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Quantum chemical simulation and low-temperature FTIR investigations of the structure and spectral characteristics of methanol monomer and dimer in an argon matrix

Pitsevich G.A.[a], Doroshenko I.Yu.[b], Pogorelov V.Ye.[b]

[a] *Belarusian State University, Minsk, Belarus*

[b] *Kiev National Taras Shevchenko University, Kiev, Ukraine*

Low-temperature FTIR spectra of methanol trapped in an argon matrix were experimentally registered and are analyzed on the base of quantum-chemical calculations of the geometry and IR spectra of methanol monomer and dimer. The calculations of spectral-structure characteristics of methanol monomer and dimer as well as the influence of Ar atoms on them were carried out using the program package WinGAMESS v. 10 okt 2010 (R1) [1] in the approximation B3LYP/cc – pVTZ. To obtain the force field adequately describing the spectral changes of the deuterated methanol molecules the program package FIREFLY v. 7.1.G [2] and approximation B3LYP/acc – pVQZ were used. The adequacy of the scaled force fields is checked by the comparison of the calculated and experimental spectra of methanol isotopomers. The calculations of the frequencies of deuterated methanol molecules were carried out using [3].

The assignment of the absorption bands in FTIR spectrum of methanol registered at 10 K to the vibrations of monomer and dimer was made taking into account the torsion-vibrational interaction. The series of the absorption bands caused by the formation of intermediate cluster structures during the sample heating from 20 to 35 K was detected. Using the results of the computer simulation of methanol dimer interaction with Ar atoms the new possible mechanism of the broad absorption bands formation in the region of torsion, deformation and stretch vibrations of the hydroxyl group of dimer donor molecule appearing at sample heating above 30 K was suggested.

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Computer simulation of the influence of the methanol dimer non-rigidity on the formation of the broadened bands in the FTIR spectra in an argon matrix

Pogorelov V.Ye.[a], Doroshenko I.Yu.[a], Pitsevich G.A.[b]

[a] *Kiev National Taras Shevchenko University, Kiev, Ukraine*

[b] *Belarusian State University, Minsk, Belarus*

Alcohol molecules attract the investigators' attention by their ability to form various cluster structures due to the intermolecular hydrogen bonds formation. The studying of such structures allows to trace the transition from individual molecules in gas phase to liquid media in more details [1, 2]. In addition to the known ones we discuss another possible mechanism of the band broadening at the example of methanol dimer. In comparison with the monomer the methanol dimers and other chain clusters as well as large cyclic and branched clusters, where to the cyclic clusters the individual molecules are added, are less rigid. Under this term we will understand the essentially larger ability to the deformation of the equilibrium geometry of the last in comparison with the monomer and, probably, the cyclic trimers and tetramers. In the case of dimer one can distinguish three parameters the deformation of which requires fewer forces. They are the change of the length of O----H bond, the value of the angle O----H-O and the relative position of the molecules determined by the rotation around the hydroxyl bond. For the studying of these problems the calculations were carried out using [3] and B3LYP/cc-PVTZ approximation. The values of the three parameters which are interesting for us varied in comparison with their equilibrium values with the step 0.01 A, 1^0 and 5^0, correspondingly. At the optimization of the dimer geometry the varied value of one of the three parameters was specified and fixed, the minimization of the energy was performed on all other parameters. For the optimized in this way geometry the IR spectrum was then calculated According to the simulation results the small changes of the non-rigid parameters of the dimer structure lead to the varying of the frequency of the hydroxyl group stretch vibration of the donor molecule on about 50 cm^{-1}, the deformational vibration – on about 25 cm^{-1}, the torsion vibration – on about 50 cm^{-1}. The similar variation of the frequency of the stretch C-O vibration does not exceed 4 cm^{-1}. The computer simulation of the interaction of argon atoms and methanol dimer in some situations was performed. In the first case two argon atoms were situated along the axes of O-C bonds from the side of carbon atoms and then the geometry of the system was optimized by all parameters. In the second case the interaction of the methanol dimer with the surface of the argon matrix was simulated. For this at one surface 9 argon atoms were situated, and at some distance from this surface – the methanol dimer. Then the positions of argon atoms at the initial surface were fixed with the possibility of their motion along the surface, and the optimization of the system geometry was performed by all parameters excluding the atoms leaving the surface. In the last case the deformed due to the relative rotation around the hydrogen bond geometry of the dimer was stabilized with two argon atoms. For the optimized systems the IR spectra were calculated. The computer simulation of the dimer interaction with argon atoms allows to vary the values of the frequency of the stretch vibration of the donor hydroxyl group almost at 20 $см^{-1}$, the frequency of the torsion vibration at 17 cm^{-1} and the frequency of the deformation vibration at 5 cm^{-1}.

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Possibile ways for predicting antineoplastic activity and mechanisms of action for the platinum complexes

Ruzhena B. Pugacheva [a], Galina N. Apryshko [a] , Ludmila V. Goncharenko [a], Natalia M. Shvets [b], Anatholy S. Dimoglo [b]

[a] *Russian Cancer Research Center, Moscow, Russian Federation*

[b] *Gebze Institute of Technologi, Gebze/Kocaeli, Turkey*

Now a great volume of data on the biological activity of co-ordination compounds of metals, especially of platinum group, is accumulated in various databases. These data can be used as informational component of computer systems, which predict biological activities of the compounds on the base of their chemical structure. The problem is that representatives of chemical structures of co-ordination compounds vary considerably from one database to another one, and in most databases chemical bonds of co-ordination compounds are either not shown at all or presented by covalent bonds. In our study, to present all structures in a unique way, the electron-topological method is used to obtain such descriptions of chemical structures of metal complexes that are eligible for computer processing. The found electronic structures of co-coordinated compounds permit to carry out researches on the structure – (antineoplastic) activity relationships and to study the mechanisms of interaction between metal complexes and possible molecular targets, in particular with DNA, by means of molecular simulation methods. In these researches, the data on the platinum complex compounds' chemical structure and antineoplastic activity are taken from the database on antitumor substances belonging to the named after N.N. Blokhin Russian Cancer Research Center of Russian Academy of Medical Science. They are used for the training sets formation in the studies on the structure – activity relationships and also in molecular simulation investigations. For the studied complexes, the sites of binding with purine and pyrimidine bases of DNA are defined. The most preferable targets for the platinum atoms' binding are nitrogen atoms of adenine and guanine in DNA molecule. In addition, molecular fragments which are responsible for the antineoplastic activity manifestation by platinum-containing complexes are defined as well.

DFT modeling of spin parameters for individual NV - centers near surface of nanostuctured diamond

V.A. Pushkarchuk[a], S.Ya. Kilin[b], A.P. Nizovtsev[b] , V.E. Borisenko[a], A.B. Filonov[a], A.L. Pushkarchuk[c,d], S.A. Kuten[d]

[a]Belarusian State University of Informatics and Radioelectronics, P. Brovka 6, 220013 Minsk, Belarus

[b]Institute of Physics NASB, Nezavisimosti Ave. 68, 220072 Minsk, Belarus.

[c]Institute of Physical – Organic Chemistry NASB, Surganova, 13 220072 Minsk, Belarus, alexp51@bk.ru,

[d]Institute for Nuclear Problems, Belarusian State University, Minsk, Belarus

For nanocrystalline diamond material surface effects play a significant role. In particular, the spin properties of the NV center itself can be corrupted by the vicinity of the surface influencing the magnetometric function of the center. Further, the surface effects reduce essentially the coherence time of the NV center spin thus reducing the sensitivity. All these problems are not studied yet. One way to get insight into them is using quantum chemical methods which have been successfully used for simulation of electronic, spin and optical properties of the NV centers in bulk diamond. Here we present the results of theoretical studies of the effect of surface on properties of the NV centers.

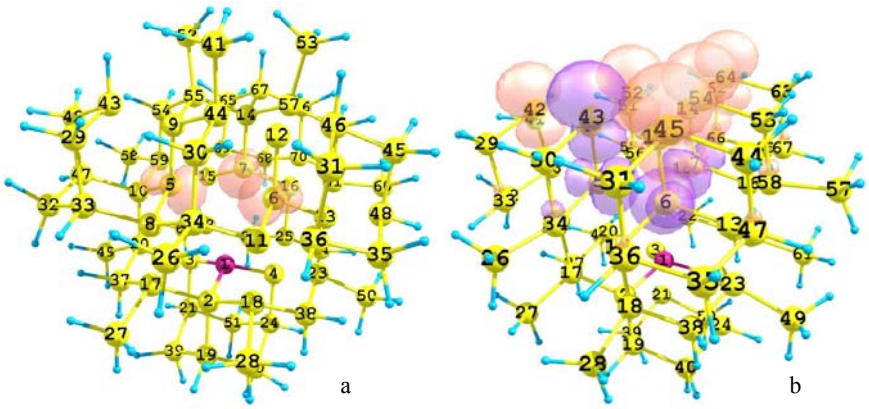

Figure 1. Spin density distributions for the "bulk" $C_{69}H_{84}[NV]^-$ and "surface" $C_{66}H_{72}[NV]^-$ clusters (a and b, respectively). Numeration of C atoms is indicated, atom N is denoted as having the number 1.

Hereinafter we are presenting results obtained for "surface" diamond cluster $C_{66}H_{72}[NV]^-$ incorporating the NV center. To construct "surface" cluster, we will consider the initial "bulk" $C_{69}H_{84}[NV]^-$ cluster (Fig. 1a), whose atomic structure has been simulated by us previously by DFT with full optimization of its geometry followed by simulation of electronic and spin characteristics of NV centers in bulk diamond. Removing three C atoms and twenty H atoms from the facet (111) of the initial cluster $C_{69}H_{84}[NV]^-$ we constructed the "non-passivated surface" cluster $C_{66}H_{72}[NV]^-$ (Fig. 1b).

Both geometric structure of clusters was optimized and the spin density distribution and magnetic resonance parameters were determined by the DFT using the B3LYP1 functional with the MINI/3-21G basis sets for singly negatively charged clusters in the triplet ground state (S=1). We used the PC GAMESS software packages developed based on the GAMESS (United States) [1].

For the "bulk" cluster the spin density is localized mainly at the three C atoms being nearest neighbors (NN) of the vacancy. For the "surface" cluster the spin density is redistributed so that it becomes also localized at the C atoms that form the first atomic layer of the (111) surface of the nanocrystal while a slightly smaller part of the density remains to be localized at three NN carbon atoms**.** The redistribution is due to appearance of surface electronic states which obviously influence the NV based magnetometry results.

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MD modeling of elastic constants of isolated carbon nanotubes

A. A. Khrutchinsky[a], S. A. Kuten[a], A. L. Pushkarchuk[a,b], V. A. Pushkarchuk[c], A. M. Saad[d], A. P. Nizovtsev[e], S. Ya. Kilin[e]

[a]*Institute for Nuclear Problems, BSU, Bobruiskaya Str. 11, 220050 Minsk, Belarus*

[b]*Iinstitute of Physical Organic Chemistry NASBSurganova Str. 13, 220072 Minsk, Belarus alexp51@bk.ru*

[c]*Belarusian State University of Informatics and Radioelectronics P. Brovki Str. 6, 220013 Minsk, Belarus*

[d]*Al-BalqaApplied University, P.O. Box 204,1Amman 11953, Jordan*

[e]*B.I. Stepanov Institute of Physics NASB, Nezavisimosti Ave. 68, 220072 Minsk, Belarus*

Carbon nanotubes (CNTs) since their discovery in 1991 [1] received much attention due to unique properties. They are currently used in mechanical, chemical and biochemical nanosensors and, in particular, in various versions of so-called "electronic nose" (e-nose) - a multi-sensor system for a rapid analysis of an air, imitating the work of human olfactory organ.

One version of the e-nose uses the fact that addition of specific molecules to the surface of the nanotube changes itsresonant frequency due to the change and redistribution of its total mass. Measuring the new CNT oscillation frequency, one can elucidate the presence of specific groups of molecules. For this reason, in this paper we present results of calculation of elastic properties as well as Raman spectra of doped and undoped CNTs, using molecular dynamics method (MD).

In the MD the functionals of a total, kinetic and potential energies are calculated.

The initial conditions are chosen so that they conform to a certain kind of pure strain, hence the functionals depend on the magnitude of this deformation. Then, using the techniques of continuum elasticity theory [2] we calculated axial compression and elastic modulus, bending strain and torsional strain.

The initial geometry of a strained state of a nanotube was prepared using the program «NanotubeModeler». The nanotubes having approximately the same radius and six chiralities have been taken to investigate dependence of their mechanical characteristics versus chirality effects.

As an example, the dependences of a nanotube total energy on the strains are given in Fig.1 for the nanotube with the chirality indicies of (8,0).

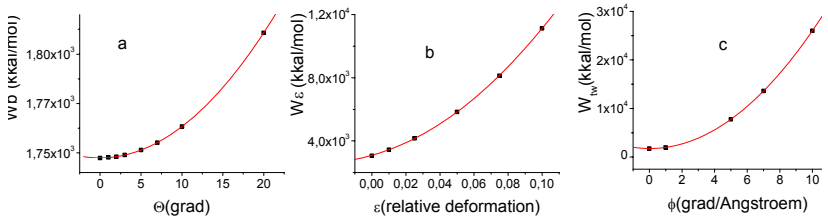

Figure 1. The calculated total energy functionals as functions of appropriate strains for: an axial compression (a), a bending strain (b), a torsional strain (c).

It was found that, the Young modulus does not depend on the chirality within the calculation errors (~ 30 %). Moreover, it does not depend on the radius of a single wall CNT within the same errors. The elastic modulus obtained coincides with the experimental data within the experimental and calculation errors (see, *e.g.* [3]).

It was also found, that addition of ten hydrogen molecules to each tube, practically does not influence the above mentioned elastic constants. This fact is caused by the weak coupling of the hydrogen molecules to the carbon frame of the nanotube.

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Molecular dynamics simulation study of *Thermus thermophilus* leucyl-tRNA synthetase with its pre- and post-transfer editing substrates

Rayevsky A. and Tukalo M.

Institute of Molecular Biology and Genetics, NAS of Ukraine, 150. Zabolotny str., Kiev, 3143 Ukraine

Aminoacyl-tRNA synthetases (aaRSs) maintain fidelity during protein synthesis by attaching amino acids to their cognate tRNAs. However, the affinity difference is not enough for the synthetases to discriminate strictly between similar amino acids. To overcome this problem, several aaRSs have evolved a specific editing activity that hydrolyze misactivated noncognate amino acids (pre-transfer editing) or mischarged tRNA (post-transfer-editing). Both reactions are depend on a tRNA cofactor and required translocation to the editing site located in the separate domain. Crystal structures of the *Thermus thermophilus* leucyl-tRNA synthetase (LeuRSTT) revealed that the same site in CP1 domain can bind analogues of both pre- and post-transfer editing substrates but the possibility of pre-transfer editing in the editing site and mechanism of editing has to be defined (1).

The main goal of this study was a comparison of features of interaction between pre-/post-transfer substrates (aminoacyl-adenylate, aminoacyl-tRNA) and amino acids of active/editing site by performing molecular dynamic (MD) simulation study. Based on the experimental and crystallographic data we selected structures (ID: 1OBC, 1OBH). Also such amino acids like leucine, norvaline and isoleucine were chosen to build complete substrates. A complex of protein with tRNA (ID: 2BTE) was prepared to show a process of editing in the CP1 domain. To obtain complexes with substrates we used molecular docking package AutoDock4.0. All structures were minimized first *in vacuo* and then in the water (model Tip3p) in the framework of force field amber99. All simulations and analyses were carried out with GROMACS 4.0.7. AM1-BCC charges were calculated for substrates using Antechamber software. To study a process of posttransfer editing the truncated editing domain (416 residues) was created. All hydrogens were added by means of H++ server and the protonation state of ionizable groups was chosen appropriate to pH 7.0. The cysteine residues which interact with the zinc ions in full structure were chosen as negatively charged cysteines (CYM). All systems were inserted in a water boxes, the layer of water (TIP3P) was equal to 10A. Then the systems were subjected to steepest descent energy minimisation for 20,000 steps. The protein backbone was frozen for 100 ps during the position restrained MD run. To obtain a relaxed state of each system a free dynamics for 20 ns were performed. Electrostatic interactions were calculated by the particle-mesh Ewald (PME) method, using 1.0 as the dielectric constant. A cut-off of 11 A was used to calculate the direct space sum for PME. The electrostatic interactions beyond 12 A were calculated in reciprocal space by the fast Fourier transform method. The SHAKE algorithm was used to restrain the bond lengths involving hydrogen atoms. The time step for integration was set to 2 fs.

After carrying out of the analysis on stability of our systems we have been started a series of MD for 5ns. The simulation of pre-transfer substrates with LeuRSTT has revealed that the non-cognate substrates bind strongly to the editing site than its cognate substrate. Among non-cognate adenylates a norvaline-adenylate binds much more better then isoleucyl-adenylate. Also, the mutation in the editing domain (valine 340 on phenylalanine) was done to estimate the importance of this position for binding of pre - and post-transfer substrates. Based on the MD and structural data a mechanism of pre- and post-transfer editing by LeuRS is proposed.

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Ab initio Modeling of Molecular Structure and Interactions in Nucleic Acid Fragments

YuryV. Rubin, Leonid F. Belous

B.. Verkin Institute for Low Temperature Physics and Engineering NAS Ukraine, Kharkov,. Ukraine; e-mail: rubin@ilt.kharkov.ua

Ab initio calculations of molecular structure and energy descriptions of nucleic acid fragments are important and useful for finding out of structure and function of nucleic acids, and also for finding out of molecular mechanisms of interaction of nucleic acids with bioactive substances. We had carried out the *ab-initio* calculations of molecular structure and energies internal interactions in a stacking dimer (TpG) (ApC) and trimer (TpGpC) (ApCpG) of nucleotide pairs ,stacking dimer, trimer and tetramer of nucleic acid base pairs, and also in the stacking dimers of base pairs with the hydrated zinc ions. Geometries of these structures were optimized by M06-2X functional of DFT method . 6-31/G* basis set was used upon optimization of the oligomer geometry. Interaction energy calculations were performed at MP2 level of theory, BSSE being taken into account and 6-31+G* basis set being applied. In the work we used Gamess , NWChem and Caussian 03 programs. Visualization of the calculations results was performed by ChemCraft Program .

The performed calculations of molecular structure of dimer and trimer of nucleotide pairs showed that interplane distance in the structures studied on the average is equal 3.2A, angle of spirality in trimer approximately equal - 30^{o}, distances between the atoms of phosphorus in nearby chains on the average - 13.1 A.. The calculations of horizontal interaction energies are performed in studied dimer and trimer .

The analysis of spatial structure (propeller and helical twist, dihedral angles) on the calculated short oligomers of nucleic acid base pairs (stacking dimer, trimer and tetramer) was performed. The analysis of internal interactions in the calculated short oligomers showed the considerable role of cross interaction in stabilization of the studied structures. The contribution of cross interactions at horizontal interactions grows as far as lengthening of oligomer. The estimations of energies of opening on outward and internal base pairs are done for the studied structures. In particular, energies of opening of external (GC) and internal (AT) pair of trimer are accordingly equal to 37.98 kcal/mol and 36.82 kcal/mol.

With the purpose to study of the influence of transition metal ions on the structure of nucleic acids we performed the calculations of molecular structure of stacking dimer of nucleic acids base pairs , and also this dimer with the ions of zinc (this dimer designed the fragment of metallized DNA, able to conduct an electric current) inculcated between bases with joining one and two hydrated zinc ions at N7 of purines.

An ab initio study of spectral parameters of the coumarins in solution and polymer matrices

I.V. Korotkova[a], T.S. Novikova[a], T.V. Sakhno[a], A. Mantel[b], N.N. Barashkov[c], Yu.E. Sakhno[d], I.S. Irgibaeva[b]

[a] *Academy of Sciences of Technological Cybernetics of Ukraine, Poltava department*

[b] *Department of Chemistry, L.N.Gumiliyov Eurasian National University, Astana*

[c] *Micro Tracers, Inc., San Francisco, California, USA*

[d] *Department of Chemistry IFM, University of Turin, Italy*

Coumarin dyes are compounds, which are ubiquitous in nature, extensively studied due to their practical applications as biological and chemical sensors, fluorescent probes and laser dyes. Understanding of their spectral-luminescence properties helps not only in the design of new molecules but also to improve performance of materials for specific application, such as luminescence solar concentrators and wavelength shifter in scintillators. Earlier we performed quantum chemical calculations and experiments which show the strong dependence of fluorescent quantum yields of some coumarin derivatives on temperature, as well as proposed a mechanism of temperature quenching fluorescence [1].

Many papers have been published on the synthesis of coumarins and various reviews are available. However, very little attention has been paid to the incorporation of coumarins into polymers, and furthermore none of the papers on coumarin-containing polymers dealt with the spectral properties. In order to study the effect of incorporation of coumarin dyes into epoxypolymer matrix we used the theoretically modeling with quantum-chemical calculations.

It is known that the electronic spectra of these molecules are influenced by their immediate environment. Among the major is a environmental factors influencing to electronic spectra, thus, analysis of solvent effects are of particular importance. In this paper we extent our previous study and examined theoretically the influence of incorporation of dyes into polymer by solvent polarity. Same coumarin derivatives (coumarin, 3,4-benzocoumarin, coumarin C504) and DCM [2-[2-[4-(dimethylamino)phenyl]ethenyl]-6-methyl-4H-pyran-4-ylidene]propanedinitrile have been selected for the present study.

The calculation of excitation energies and oscillator strengths of molecules were performed using of TD-DFT method with the B3LYP functional and the 6-31G basis set. The dependence of absorption maxima on solvent polarity was treated quantitatively using the solvent parameters K (Kirkwood-Onsager constant). The theoretically calculated results show a bathochromic shift which is observed upon increasing the polarity of the solvent for these dyes indicating $\pi \rightarrow \pi^*$ transition and a hypsochromic shift indicating $n \rightarrow \pi^*$ transition. The dielectric constant (ε) of epoxypolymer is 3,0-6,1 and we choose the solvents with corresponding dielectric constant (from chloroform to acetonitrile). By changing the solvent polarity in this region a large spectral shift of about 23 and 44 nm for C504 and DCM in the absorption spectra is observed. In case of coumarin and 3,4-benzocoumarin this spectral shift is ~ 4 nm. The results were compared with experimental data [2]. On the basis of calculated results we conclude that TD-DFT method of calculation is in a good agreement with experimental absorption spectra of coumarin C504 and DCM in epoxypolymer matrix.

In summary, we show the possibility of using quantum-chemical modeling not only for calculation of energy parameters for coumarin dyes, but also for prediction of spectral properties of dyes incorporated into polymer matrix.

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Absorption centeres of coloured PTFE

E.M. Konova [a], S.A. Khatipov [a], V.G. Klimenko [a], Yu.E. Sakhno [b], S.T. Sychkova [c], T.V. Sakhno [d]

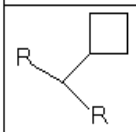
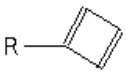
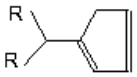
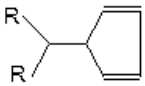
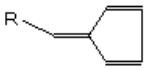
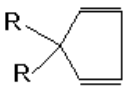
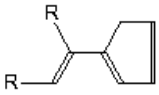
[a] *L.Ya.Karpov Institute of Physical Chemistry, 105064, Moscow, Russian Federation*

[b] *Department of Chemistry IFM, University of Turin, Italy.*

[c] *Poltava University of Economics and Trade 36014, Poltava, Ukraine*

[d] *Academy of Sciences of Technological Cybernetics of Ukraine, Poltava department, 36007 Poltava, Ukraine, sakhno2001@mail.ru*

Table TD-DFT Calculations on the Lowest Energy Transitions

Molecules	transition energy (eV)	Oscillator Strength	transition (dominant)
	5.7448 6.4207 6.9238 7.1546 7.4671	0.0006 0.0072 0.0047 0.0032 0.0019	HOMO → LUMO HOMO-1 → LUMO HOMO-2 → LUMO HOMO-3 → LUMO HOMO-4 → LUMO
	1.6878 3.4538 4.3948 4.7531 5.6023	0.0014 0.0044 0.0023 0.0341 0.0030	HOMO → LUMO HOMO → LUMO+1 HOMO → LUMO+2 HOMO → LUMO+3 HOMO → LUMO+4
	3.1165 5.1829 5.3526 5.8859 6.2056	0.0236 0.0002 0.0017 0.0121 0.1070	HOMO → LUMO HOMO → LUMO+1 HOMO → LUMO+1 HOMO → LUMO+2 HOMO-1 → LUMO
	3.4383 5.4792 5.9268 6.0698 6.2804	0.0741 0.0020 0.0056 0.0074 0.0448	HOMO → LUMO HOMO-1 → LUMO HOMO → LUMO+2 HOMO-3 → LUMO HOMO-2 → LUMO
	1.6055 4.7910 5.0385 5.3352 5.5576	0.0020 0.4830 0.0011 0.0000 0.0007	HOMO → LUMO HOMO-1 → LUMO HOMO → LUMO+1 HOMO → LUMO+2 HOMO-2 → LUMO
	3.7860 5.2527 5.5670 5.7469 6.0727	0.0330 0.0005 0.0010 0.0084 0.0017	HOMO → LUMO HOMO → LUMO+1 HOMO → LUMO+3 HOMO → LUMO+2 HOMO → LUMO+4
	2.9122 4.5345 5.4958 5.6655 5.8127	0.2036 0.0045 0.0000 0.0005 0.3341	HOMO → LUMO HOMO-1 → LUMO HOMO-2 → LUMO HOMO → LUMO+2 HOMO → LUMO+1

The PTFE films exposed to γ-irradiation near the melting point change it coloring and exhibit intense fluorescence [1]. Earlier we have proposed hypothesis of initiation mechanism of fluorescent absorbance centers caused by polyene structures formation [2]. It has been established that, such factors as ratio of different types of optical emission centers and sample coloring are strongly depend on conditions of sample irradiations. The optical centers responsible for sample coloring and for appearance of fluorescent properties are two different types of compounds with conjugated bonds. Recently authors [3] have proposed theory of cyclic compounds formation at the superficial layer of PTFE films. In the present work we've reported the results of theoretical calculations of cyclic structures optical centers (Table.R=CF_3-$(CF_2)_n$ -) that absorb in visible region. Cyclic compounds with conjugated triple bonds absorb in visible spectrum range and can be a cause of color appearance in irradiated PTFE. In the visible range the absorption bands are responsible for formation of conjugated compounds with four or five carbon atoms.

[1] Khatipov, S. A., Nurmukhametov, R. N., Seliverstov, D. I., Sergeev, A. M., Polymer Science, Ser. A. 2006.48, 153–158.

[2] Yu.E. Sakhno, V.G. Klimenko, et al., Polymer Science, Ser. B, 50 (2008), 117-119.

[3] Lei Li, Paul M. Jones, Yiao-Tee Hsia, Applied Surface Science, Volume 257, Issue 9, 15 February 2011, Pages 4478-4485

Theoretical study of inter and intramolecular proton transfer in N-hydroxy amidines

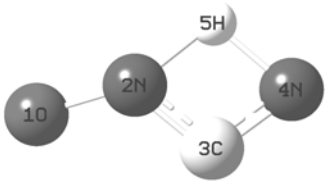
A. Samzadeh, H. Tavakol

Department of Chemistry, University of Zabol, Zabol, Iran; e-mail: arsamzadeh@yahoo.com

N-hydroxy amidine [1] is an important and useful group in synthesis of various compounds[2] in organic chemistry and some other applications can be considered for this group [3].

This functional group is found in two tautomeric forms; one is amino-oxime (tautomer **a**) and the other is imino-hydroxylamine (tautomer **b**). In our study, at first, we optimized the structure of each tautomer and after that; IR frequencies, energies and other molecular parameters of tautomers have been computed by quantum mechanic calculations, using Gaussian 03 with 6-311++G** basis set in both ab initio and density functional methods with basis set extrapolation and MP2 correction of energy. The result found in both methods shows that the tautomer **a** is more stable than the tautomer **b**.

In next step, we guessed the structure of transition state for each pair of tautomers and optimized by QST3 calculations. The strusture of shered part of all transition states showed in below. After all, we computed the energy and molecular parameters of transition states. Our finding shows that, the energy difference between two tautomers is low but the barrier energy found in traversing of each tautomer to another one is high.



We say that this conversion can be considered as a kind of 1,3-sigmatropic rearrangement of hydrogen. As we know, such thermal rearrangement for hydrogen is forbidden and our finding confirms this postulate.

[1] Kakanejadifard A., Toosi-Jamali H., Alboghobeish F., *Polish J. of Chemisty,* **81**, 1541 (2007).
[2] Kakanejadifard A., Delfani F., Ranjbar B., *Iranian J of Chem & Chemical Eng,* **22**, 13 (2003).
[3] Ghiasvand A. R., Shadabi S., Kakanejadifard A., *Chemia Analityczna,* **52**, 125 (2007).

Molecular dynamics study of crystallographic and theoretically found conformations of human serum albumin

I.E. Shchechkin, T.O. Hushcha

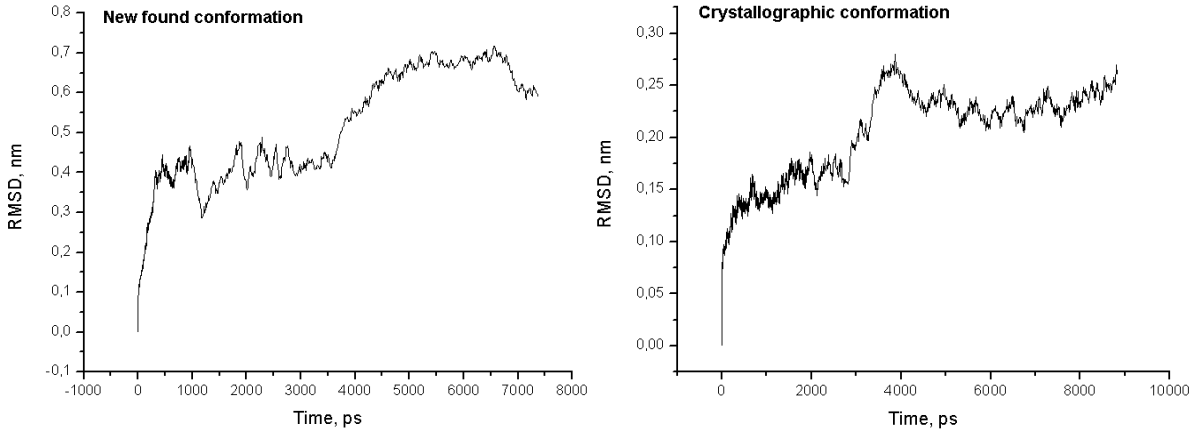
Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Science of Ukraine, 1 Murmanska str., 02660, Kiev-94, Ukraine; e-mail: shch406@bpci.kiev.ua

Loops and loop-like structures play considerable role in protein functionality, serving as flexible sites or gates to the active sites. We investigated the role of these structural elements at human serum albumin (HSA), the most widespread protein of the blood circulation system, which adsorbs many fatty acids, metabolites, drugs and is used to test new medicines. HSA is a monomeric globular protein consisting of 585 residues and structurally constructed of three similar domains *I-III,* each of them, in turn, consisting of two subdomains *a* and *b*. Adjacent domains are bonded with loop-like structures (LLS). There exist more then ten fatty acid binding sites in HSA molecule, and the binding is accompanied with drastic change in mutual disposition of the domains. So the question arises – what structural changes of LLSs are associated with such considerable mutation of HSA spatial structure.

In our previous studies we carried out theoretical conformational analysis for the following model system of HSA: rigid subdomain *Ia* - flexible LLS 106-177 - rigid rest of the molecule. This yielded stable conformation, which considerably differs in spatial structure, but is close in energy to the crystallographic one. To obtain the more realistic picture of the functioning of the new found conformation (NFC) in the present study we simulated dynamics of the same model system, starting from this conformation. For comparison, we modeled dynamics of crystallographic conformation (CGC), which coordinates were taken from Brookhaven Data Bank, identifier 1AO6.

Simulation was performed with *Gromacs 4.03* program package, in space of atomic Cartesian coordinates, in frame of periodic boundary conditions, the molecule being encompassed with 33949 water molecule for NFC specimen and 32928 water molecules for CGC one (this corresponds to 0.5 nm of water layer width). Particle Mesh Evald algorithm for electrostatic interaction evaluation was used.

The movement was investigated during 8.82 ns for NFC and 7.38 ns for CGC. NFC specimen appears to be unstable under the dynamics modeling algorithm. So it was initially underwent simulated annealing procedure during 500 ps starting from zero temperature to 298K. After this the both specimens behaved similarly: they had initial equilibration stage during about 500 ps, then oscillation, then slight conformational transition and oscillation in the new state again. Scale of the whole RMSD deviation is 2.5 greater for NFC, which seems to be natural. However, shelf-like structure of RMSD curve for NFC shows that theoretically found stationary point at the potential energy surface corresponds to really existing stable spatial structure.



All the calculations were performed at computer cluster, organized with help of *Intel* company in computer center of Kiev Shevchenko National University.

Evaluation of molecular volume in terms of abstractly defined molecular surface

I.E. Shchechkin, T.O. Hushcha

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Science of Ukraine, 1 Murmanska str., 02660, Kiev-94, Ukraine; e-mail: shch406@bpci.kiev.ua

New method is proposed for evaluation of molecular volume of solvated protein on the basis of atomic coordinates of its atoms. The method utilizes the approach defining the volume confined inside of specified molecular surface. Using this approach molecular surface is partitioned into fragments serving the bases for the cones all having common vertex, located anywhere inside the surface. Volume of the molecule is calculated as the sum of volumes of the cones.

Surface of molecule is usually defined as the surface of the van der Waals spheres of its atoms accessible to water molecule probe. Unlike this way we propose approach defining the elements of the molecular surface using the ideas of the contemporary solvent accessible surface evaluation techniques. In these techniques the elements of molecular surface are introduced in an abstract way without partitioning of the preliminary constructed surface. We define molecular surface as the set of elements, each one having square and orientation vector as its attribute. Specifically, the space around each atom is divided into four identical cones oriented in tetrahedral symmetry relatively to the center of the atom, thus four surface elements each associated with each cone correspond to each atom. Normal vector of a surface element orientation is one along the corresponding cone axis. Square of each surface element ΔS_{ik} is defined proportional to amount of free space A_{ik} within the cone k of atom i:

$$\Delta S_{ik} = C_i A_{ik} .$$

Amount of free space A_{ik} is evaluated as:

$$A_{i,k} = \frac{\rho_i^* - \rho_{i,k}}{\rho_i^*} \pi \left(r_{H_2O} + r_i \right)^2 \quad , \qquad (1)$$

where r_i – van-der-Waals radius of atom i, ρ_{ik} – density of neighbor atoms in the cone k of atom i, ρ^*_i – limitary neighbor density, when free space in the cone becomes zero; if $\rho_i > \rho^*_i$, the cone is considered as "nonsurface" and the corresponding square is assumed to be zero.

In turn, the neighbor density for cone k of atom i is evaluated according to the formula:

$$\rho_{i,k} = \sum_j^{m_{i,k}} G_{ij} \, , \; G_{ij} = \exp\left[-\alpha_i \frac{d_{ij}^2}{\left(r_{H_2O} + r_j \right)^2} \right], \qquad (2)$$

where:

$m_{i,k}$ – the number of neighbor atoms whose centers belong to the cone k of atom i;

d_{ij} – distance between centers of i and j atoms;

r_j – van der Waals radius of j neighbor of atom i;

r_{H2O} – radius of water molecule (1.4 Å).

C_i, ρ^*_i, r_{H2O}, α_i and d_{cut} – are the parameters to be adjusted.

The advantage of our approach consists in its flexibility enabling different kinds of volume, for instance, partial, internal, excluded and so on, to be calculated with the same algorithm using suitable adjustable parameters.

In this report we apply the developed method for calculation of protein partial volume in solution. We find remarkable agreement of the calculated volumes with corresponding experimental data.

The influence of sugar switches dynamics on the formation of bending deformation of DNA on base pair level

Ya.V. Shashel[a], A.V. Shestopalova[b], M.Y. Tolstorukov[c]

[a] *V.N. Karazin Kharkiv National University, Kharkov, Ukraine*

[b] *Usikov Institute for Radiophysics & Electronics NASU, Kharkov, Ukraine*

[c] *Harvard-Partners Center for Genetics and Genomics, Boston, USA*

Structural deformability of DNA and dynamics of switches of nucleotide sugar puckering is an important mechanism of indirect recognition in protein-nucleic acid complexes. Molecular dynamics simulation is the one of the most informative way to get the ultimate detail concerning individual particle motions as a function of time and to obtain information that is not accessible from experiment.

In our work the influence of sugar switches dynamics on the formation of angle propeller twist describing bending deformation on base pair level was investigated. The DNA (containing 12 basepairs) was built using the crystal structure from the PurR complex. We analyzed correlations of sugar switches and base-pair parameter in 10 ns of unrestrained molecular dynamics simulation of 10 base pairs (namely 6 CG and 4 AT). Marked correlations between dynamics of the bases (Propeller twist) and switches of sugar puckering from the C2'-endo conformation, representative of B-DNA, to the C3'-endo conformation, representative of A-DNA were observed. The absolute value of Propeller twist angle for AT pair is higher on the whole, than for GC pair, and it is explained by the big bend of A-tracts; availability of AT base pairs, which can be met every 4-6 pairs, leads to the DNA bend and this bend is not concerned with protein. The frequency of switches of sugar puckering from B-DNA into A-DNA influences more on GC pair, than on AT pair. That is why the dynamics of sugar-phosphate backbone of cytosines in the of kinked base-pair step CpG is basic for occurrence of kink. Such dynamics leads to rotation of nitrogenous bases around glycosidic linkage χ and the formation of Propeller twisting angle, and in the same times means the opening of base pair into minor groove and factually formation a small kink, which is not concerned with DNA bend. It was shown that the Propeller twist angle depends both on base pair and on conformation of sugar. The sugar switches of pyrimidines affect significantly propeller twist angle at the base-pair level.

The construction and the analysis of the new 3D QSAR descriptors

A.M. Shestov, A.V. Koptsova, M.I. Kumskov

Department of Computational Mathematics, Faculty of Mechanics and Mathematics, Lomonosov Moscow State University, 119992 Moscow, Russian Federation; e-mail: qsar_msu@mail.ru, shestov.msu@gmail.com

Introduction

Solution of the «structure – property» problem or QSAR-problem (Quantitative Structure-Activity Relationship) [2] consists of two stages: stage of the description and stage of the construction of the classifying function [2, 3]. The quality of the solution very much depends on the descriptors chosen. The method, proposed in this paper, constructs descriptors according to the "key-lock" model[4]. These descriptors are easy to interpret and do not need alignment of the molecule (unlike the COMFA method). This method is based on the segmentation of the compound's molecular surface[1], and takes into account its local geometric and physico-chemical properties. The results obtained using these descriptors and k-NN classification are given.

QSAR problem statement

Descriptor is such a property, which can be calculated for every molecular graph. *The alphabet of descriptors* is a set of all descriptors used for the training set describing. Let the alphabet of descriptors consists of M elements. *Feature vector* of the molecular graph *G* is called a vector $x = (x_1, \ldots x_M) \in R^M$, where x_i - the value of the i-th descriptor computed for *G*.

Method of descriptors constructing

The first step is to find "singular" points p_i on the molecular surface. Then we assign each singular points p_i a type t_{1i} according to its local geometric and physico-chemical properties. Then we assign each pair of singular points (p_i, p_j) a type t_{2i} according to the t_{1j}, t_{1i} and the distance between p_i and p_j. The value of the k-th descriptor computed for a molecular graph *G* is a number pairs of singular points of type k on the molecular surface of *G*.

We consider bulges and cavities to be singular points. The algorithm finds them according to the fact, that molecular surface is an association of spheres and toruses parts. So we divide the molecular surface into segments of different curvature and take a center of each segment as a singular point.

Results

This algorithm was implemented and applied to three samples – glikosides (the best result 0.86), pirimidines (the best result 0.89), and toxic compounds (the best result 0.52).

[1] M. L. Connolly, "Analytical molecular surface calculation", J. Appl. Crystallogr. 16 (1983) 548–558.

[2] M.I. Kumskov, E.A. Smolensky, L.A. Ponomareva, D.F. Mityushev, N.S. Zefirov. Systems of Structural Descriptors for QSAR Problem Solving// Proceedings of the Academy of Science – 1994. - Vol. 336, No. 1. - P. 64-66 (in Russian).

[3] Prokhorov E.I., Perevoznikov A.V., Voropaev I.D., Kumskov M.I., Ponomareva L.A. - Search representations of molecules and methods of prediction activity in the problem of "structure-property" // Reports of the 14th All-Russian Conference "Mathematical Methods for Pattern Recognition" MMRO-2009. - Moscow: MAX Press. - 2009. - S. 589-591 (in Russian).

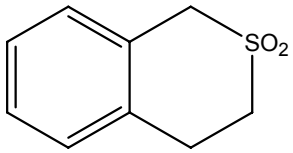
Molecular structure and ring inversion profile for heterocycle in 1H-isothiochromen-4(3H)-one 1,1-dioxide

Svetlana V. Shishkina[a], Olena O. Shyshkina[b], Julian M. Volovenko[b], Oleg V. Shishkin[a]

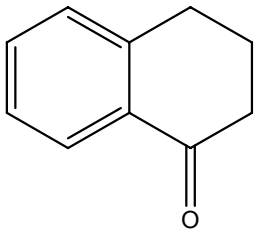
[a] STC "Institute for Single Crystals," National Academy of Sciences of Ukraine, 60 Lenina ave., Kharkiv 61001, Ukraine; e-mail: sveta@xray.isc.kharkov.com

[b] Kyiv National Taras Shevchenko University, 64 Volodymirska str., Kiev, 01033, Ukraine

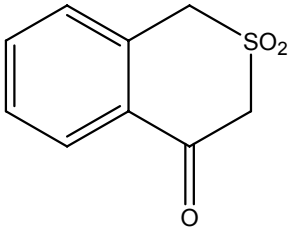
Cyclohexene ring possesses very unusual ring inversion profile which is completely flattened in the area of boat conformation as transition state. Results of calculations by MP2/6-311G(d,p) method demonstrate that annelation of cyclohexene by benzene ring results in significant stabilization of boat conformation which corresponds to minimum on the potential energy surface. Similar situation is observed for tetraline analogues where one methylene group is replaced by SO_2 fragment. However presence of exocyclic carbonyl bond leads to disappearance of minimum on the potential energy surface corresponding to boat conformations. Moreover, ring inversion profile becomes normal without top-flattened character.



Isothiochroman 2,2-dioxide



3,4-Dihydro-2*H*-naphthalen-1-one



2,2-Dioxo-2λ^6-isothiochroman-4-one

In the case of presence of both carbonyl group and SO_2 fragment tetrahydroaromatic ring adopts half-chair equilibrium conformation as it was established by both X-ray diffraction study and quantum-chemical calculations. Ring inversion profile has an intermediate character between tetraline and tetralone molecules with two minima on the potential energy surface corresponding to half-chair conformations and top-flattened ring inversion profile.

The n-σ* hyperconjugation in HONO and MeONO molecules containing the protocovalent bond

Angelika I. Slabko[a,b], Svitlana V. Shishkina[a], Oleg V. Shishkin[a], Slawomir Berski[c], Zdzislaw Latajka[c]

[a] *STC "Institute for Single Crystals," National Academy of Sciences of Ukraine, 60 Lenina ave., Kharkiv 61001, Ukraine; e-mail: aslabko@xray.isc.kharkov.com*

[b] *National Technical University "Kharkiv Polytechnical Institute", 21 Frunze Str., Kharkiv, 61002, Ukraine*

[c] *Faculty of Chemistry, University of Wroclaw, 14 F.Joliot-Curie, Wroclaw 50-383, Poland*

Hyperconjugation is a wide and useful concept in chemistry which allows to explain some structural effects like the anomeric effect in saturated molecules. According to traditional viewpoint this effect is much weaker as compared with π-π or n-π conjugation. However recent theoretical investigation of derivatives of heteroatomic analogues of butadiene [1] demonstrated influence of n-σ^* hyperconjugation between lone pair of heteroatom and antibonding orbital of single C(sp^2)-C(sp^2) bond on geometry of molecule in spite of presence of π-π conjugation.

The molecules of nitrous acid (HONO) and its methyl derivative have a lot of lone pairs. There are the n-σ^* interactions between lone pair and double bond or antibonding orbital in these molecules along with n-π conjugation. It can assume they may significantly influence geometrical parameters of these molecules.

Results of calculations by MP2/aug-cc-pvtz method demonstrate the shortening of the O-N bond length in s-cis conformer (Δl=0.042 Å) as compared to s-trans conformer for both molecules. Careful analysis of intramolecular interactions in conformers of HONO and MONO using NBO theory reveals that the total energy of bonding interactions is higher as compare with total energy of antibonding interactions in cis-conformer. The opposite situation is obtained for trans-conformer. It is reflected on bond length.

The influence of each of intramolecular interactions on geometry of s-cis and s-trans conformers of HONO was investigated using method of shielding of lone pair by BH_3 molecule.

[1] Shishkina, S.V.; Shishkin, O.V.; Desenko, S.M.; Leszczynski, J. J.Phys.Chem.A, 2008, **112**, 7080.

DFT study of CO_2 - zeolite interactions: adsorption and molecular dynamics

[a]Smykowski Daniel, [a]Szczygieł Jerzy, [b]Szyja Bartłomiej

[a]Wrocław University of Technology, Division of Chemistry and Technology of Fuel; e-mail: daniel.smykowski@gmail.com

[b]Technische Universiteit Eindhoven, P.O. Box 513, Netherlands

Carbon dioxide emission is a consequence of combustion processes, where use of fossil resources has main contribution. Apart from having negative effect on the climate, carbon dioxide is a useless waste. At the moment, there is no technology for effective conversion of CO_2 into useful and highly demanded products in order to utilize large amounts of CO_2.

A large variety of solutions for carbon dioxide utilization has been proposed, including: underground and underwater storage, CO_2 reforming of methane, electrochemical reduction, conversion to carbon monoxide and methanol. An interesting concept is conversion of carbon dioxide into fuel-like hydrocarbons, that could be used as fuel components. This would enable production of fuels and saving of fossil resources.

This work is focused on studying interactions between CO_2 molecule and modified zeolite structures. The scope of the study includes docking simulations with self-developed tool and molecular dynamics using DFT method. This allowed to characterize the influence of the presence of cations on interactions between CO_2 molecule and zeolite structure.

Structures used in the simulations were created by modification of zeolite structures. Two selected Si atoms were replaced with two Al atoms and, for charge compensation, a +2 cation was introduced (Cu^{2+}, Zn^{2+}, Pd^{2+}, Ni^{2+}, Co)

The results show that, the presence of a cation in the zeolite structure has important influence on adsorption energy. The structures, that contain cation are able to adsorb CO_2 stronger.

It is remarkable, the smaller is the distance between CO_2 molecule and cation, the lower is the adsorption energy. This means that the adsorption is stronger close to the cation. This effect has interesting consequences in MD results - CO_2 molecule, when close to cation, is "locked" in one position, whereas CO_2 far from cation can make a rotation. In this way, cation can be described as adsorption active center. Adsorption energy magnitudes are typical for chemisorption (~1eV).

[1] J.H. Edwards: Potential sources of CO_2 and the options for it's large-scale utilisation now and in the future, Catalysis Today (1995), Vol.23, s. 59-66

[2] K. M. K. Yu, I. Curcic, J. Gabriel, and S. C. E. Tsang: Recent Advances in CO_2 Capture and Utilization, ChemSusChem 2008, 1, 893 – 899

[3] A. J. Morris, G. J. Meyer, E. Fujita: Molecular Approaches to the Photocatalytic Reduction of Carbon Dioxide for Solar Fuels, Accounts of Chemical Research, 2009

[4] J. Szczygieł, B. Szyja: Wybrane metody chemii obliczeniowej w projektowaniu katalizatorów heterogenicznych, Oficyna Wydawnicza Politechniki Wrocławskiej, 2006

Calculations were carried out using resources of Wrocław Center of Networking and Supercomputing (WCSS).

Study on Decomposition of Nitrous Oxide on Al–ZSM-5: MP2 versus DFT/B3LYP

Vitaly Solkan

N. D. Zelinsky Institute of Organic Chemistry, RAS, 119991 Moscow, Leninskii pr. 47. Russian Federation

Nitrous oxide (N_2O) is a potent greenhouse gas and contributes to ozone layer depletion. This has prompted the development of several abatement technologies based mainly on the catalytic decomposition. Recently we presented DFT/B3LYP study of the interaction of nitrous oxide with Ga/ZSM-5 and GaO/ZSM-5 [1]. The active centers were taken to be mononuclear $[Ga]^+$ and $[Ga{=}O]^+$. We shoved that the first step of N_2O decomposition involves the formation of $[GaO]^+$ and the release of N_2. The metal-oxo species produced in this step then reacts with N_2O again, to release N_2 and form $[GaO_2]^+$. The calculated activation energies for N_2O dissociation in Ga-ZSM-5 and GaO-ZSM-5 are 22.2 and 24.9 kcal/mol, respectively. In the present work we have performed a detailed theoretical study of the mechanisms of nitrous oxide dissociation in Al-ZSM-5, AlO-ZSM-5, and AlO_2-ZSM-5 using post-Hartree-Fock calculations at MP2/6-31+G(d) and DFT/B3LYP/6-31+G(d) computational levels. The active centers were taken to be mononuclear $[Al]^+$, $[Al{=}O]^+$, and $[AlO_2]^+$ and the surrounding portion of the zeolite was represented by a 3T cluster, namely $[AlSi_2O_4H_8]^-$. The first elementary step of N_2O decomposition involves the formation of $[AlO]^+$ and the release of N_2. The metal-oxo species produced in this step then reacts with N_2O again, to release N_2 and form $[AlO_2]^+$. The calculated activation energies at DFT/B3LYP level for N_2O dissociation on Al-ZSM-5 and AlO-ZSM-5 are 9.86 and 15.07 kcal/mol at 298 K, respectively. The third elementary step of N_2O decomposition on AlO_2-ZSM-5 involves the formation of $[AlO_3]^+$ and the release of N_2. The calculated activation energy at DFT/B3LYP level for N_2O dissociation on AlO_2-ZSM-5 is 18.24 kcal/mol. Four-order perturbation theory (MP4// DFT/B3LYP) predicts that the activation barriers for nitrous oxide dissociation at 298 K on Al-ZSM-5, AlO-ZSM-5, and AlO_2-ZSM-5 are 13.97, 17.89, and 32.71 kcal/mol, respectively. The calculated energy for desorption of singlet O_2 from the $3T^-[OAl(O)_2]^+$ cluster at DFT/B3LYP level is 57.8 kcal/mol. When one takes into account the entropy gained upon desorption of singlet O_2, the contribution of entropy to the free energy of desorption is $T\Delta S$ =10.8 kcal/mol at 298 K. The calculated activation energies at MP2/6-31+G(d) level for N_2O dissociation on Al-ZSM-5 and AlO-ZSM-5 are 13.90 and 26.87 kcal/mol at 298 K, respectively. The calculated activation energy at MP2/6-31+G(d) level for N_2O dissociation on AlO_2-ZSM-5 is 38.25 kcal/mol. The calculated energy of the singlet oxygen desorption from $3T^-[AlO_3]^+$ cluster ΔH (298 K)=+46.4 kcal/mol at MP2/6-31+G(d) level is significantly higher than the barriers of oxidation reactions. When one takes into account the entropy gained upon desorption of singlet O_2, the contribution of entropy to the free energy of desorption is $T\Delta S$ =11.0 kcal/mol at 298 K. Thus, the method B3LYP seriously underestimates the activation energy for N_2O dissociation on Al/AlO/AlO_2-ZSM-5. The problem here, of course, is that current functionals do not correctly describe the dispersion energy, which is well described by MP2 calculations. Therefore, further DFT investigations are needed that are validated by comparison to available experimental data or high-level quantum chemistry methods that treat electron correlation more accurately [2].

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MP2 Study of the Mechanism of Formation of the HOO Radical in the ($CF_3COOH + {}^3O_2$) System

Vitaly Solkan

N. D. Zelinsky Institute of Organic Chemistry, RAS, 119991 Moscow, Leninskii pr. 47. Russian Federation

Trifluoroacetic acid always contains a certain amount of molecular oxygen dissolved in it, and the question arises of the mechanism of its activation. We therefore theoretically studied the possibility of formation of electron acceptor and electron donor centers in trifluoroacetic acid and their interactions with molecular oxygen in the ground state by the ab initio Möller–Plesset second order perturbation theory method (MP2) and the CBS-QB3 method. The main reaction in trifluoroacetic acid resulting in the formation of the protonated center is autoprotolysis. The CBS-QB3 calculations with taking medium effects into account by the PCM method showed that the autoprotolysis of trifluoroacetic acid was moderately endothermic (13.57 kcal/mol). It follows that anhydrous trifluoroacetic acid can contain the $CF_3CO_2H_2$ (+) and CF_3COO (-) solvated ions. Modeling of the interaction of molecular oxygen in the ground state with $CF_3CO_2H_2$ (+) by the MP2/6-311++G(*d*, *p*) method shows that the potential energy surface contains the ($CF_3CO_2H_2$(+) … $^3O_2$) complex with a short H-bond *r*(O…H) = 1.869 Å. The calculated complex formation energy is 2.97 kcal/mol. The CBS-QB3 method was used to calculate the thermal effect of the reaction $CF_3CO_2H_2$ (+). + $^3O_2$ = CF_3COOH + O=O–H (+)(T) taking into account medium effects by the PCM method. The reaction was found to be strongly endothermic, ΔH(gas) = 66.95 kcal/mol and ΔH(sol) =55.35 kcal/mol in the gas phase and solution, respectively. The potential energy surface of (CF_3COO(-) …$^3O_2$) calculated by the MP2/6-311++G(*d*, *p*) method contains a minimum corresponding to a weakly bound complex of $^3O_2$ with the anion with distances of 3.311 and 3.709 Å between the oxygen atoms of the carboxyl group and $^3O_2$ oxygen atoms . The calculated complex formation energy for this complex is 1.72 kcal/mol. The CBS-QB3 calculations were performed with taking into account medium effects by the PCM method to determine the heat effect of the reaction CF_3COO(-) + $^3O_2$ =CF_3COO• + O=O–• . The reaction was found to be strongly endothermic, ΔH(gas) = 95.31 kcal/mol and ΔH(sol) =80.19 kcal/mol in the gas phase and solution, respectively. According to MP2/6-311++G(*d*, *p*) calculations, the bridge stabilization of oxygen bound with both the cation and anion is much more favorable energetically. Studies of the potential energy surface of the joint molecular system ($CF_3CO_2H_2$ (+) …$^3O_2$… CF_3COO (-)) show that the proton experiences activationless transfer from the cation to the $^3O_2$ molecule accompanied by electron transfer from the CF_3COO(-) anion. An analysis of spin density distribution calculated by both the UHF and UMP2 methods provides convincing evidence of the stabilization of two radicals in the (CF_3CO_2…OOH…O=C(OH)CF_3) complex observed on the potential energy surface. According to the calculation results, the geometric and electronic structure of the OOH fragment in the complex in the triplet state corresponds to a perturbed hydroperoxyl radical. The heat effect of the formation of the complex of the hydroperoxyl radical with the CF_3COOH molecule and CF_3COO• radical: (CF_3COOH_2 (+) + $^3O_2$ + CF3COO(-)) = (CF_3COO•+OOH•+CF_3COOH) (T), was calculated by the MP2 method. Complex formation was found to be substantially exothermic in the gas phase, ΔH(gas) = –82.74 kcal/mol.

The theoretical analysis performed leads us to conclude that active intermediates in the oxidation of various substrates by molecular oxygen in trifluoroacetic acid can be hydroperoxyl radicals or CF_3COO• + OOH• radical pairs.

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Proton solvation and self-dissociation of 100% perchloric acid: The quantum-chemical analysis

Vitaly Solkan

N. D. Zelinsky Institute of Organic Chemistry, RAS, 119991 Moscow, Leninskii pr. 47. Russian Federation

It is quite clear that the specific properties of superacids arise from the unusual properties of solvated protons instead of the high degrees of dissociation. For instance, the dissociation constant of anhydrous sulfuric acid is equal to only 10^{-4} whereas for liquid hydrofluoric acid it is as low as 10^{-10}. Therefore, since both HF and H_2SO_4 behave as superacids only in anhydrous solution, extremely high chemical activity of protons is associated with the relatively weak solvation in comparison with solvation by the more basic water molecules [1-5]. In the present work we have performed a detailed theoretical study of the proton salvation in 100% perchloric acid.

Ab initio quantum-chemical calculations of solvation energies of $H_2ClO_4^+$ cation and ClO_4^- anion by one molecule of perchloric acid in the gas phase have been performed at the MP2 level using the 6-311++G** basis set. Additional contributions to the solvation energy of the acid arising from electrostatic interactions with the surrounding molecules in the liquid were estimated in the framework of the polarizable continuum model (PCM or IPCM models). Together with the experimental values for the energies of protonation and deprotonation of perchloric acid in the gas phase the calculated solvation energies were then used to estimate the heats of self-dissociation of the liquid perchloric acid and of proton solvation by the anhydrous acid. An almost quantitative agreement of the calculated heat of self-dissociation with the experimental value indicates a rather high accuracy of the calculations. A remarkable feature of the anhydrous perchloric acid is a low value of solvation energy of protons that is about 30 kcal/mol smaller than in the aqueoussolution. This result explains why anhydrous perchloric acid, despite the low value of dissociation constant, behaves as a superacid [6].

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DFT/B3LYP Study of the Mechanism of Oxodiazonium Ion Generation

Vitaly Solkan

N. D. Zelinsky Institute of Organic Chemistry, RAS, 119991 Moscow, Leninskii pr. 47. Russian Federation

Recently [1], a new method for the synthesis of [1,2,5]oxadiazolo[3,4-c]cinnoline 5-oxides which involves reaction of 3-(nitramino)-4-(R-phenyl)furazans or their *O*-methyl derivatives with electrophilic reagents has been developed. It is suggested, that in these reactions the treatment of nitramines or their *O*-methyl derivatives with electrophilic reagents results in formation of oxodiazonium ion, which takes part in the intramolecular S_EAr reaction with the aryl group. The theoretical investigation using DFT/B3LYP/6-311G(d,p) of the associated molecular system (*O*-methylated 3-nitramino-4-phenylfurazan + $[H_3SO_4]^+$) and localization of the stationary points at the PES including the oxodiazonium ion (Fig. 1) allows to calculate the thermodynamic parameters of the sequence of cascade elementary reactions resulting in the [1,2,5]oxadiazolo[3,4-c]cinnoline 5-oxides formation. The theoretical analysis performed leads us to conclude that active intermediates in the formation of [1,2,5]oxadiazolo[3,4-c]cinnoline 5-oxides can be oxodiazonium cation.

Fig. 1. Structure of the (*O*-methylated 3-nitramino-4-phenylfurazan + $[H_3SO_4]^+$) complex optimized by the B3LYP/ 6-311G(*d*, *p*) method.

Fig. 2. Structure of the σ-complex optimized by the B3LYP/ 6-311G(*d*, *p*) method.

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Toward reliable carbon nanotube (CNT) – molecular hydrogen interaction modeling via density functional theory (DFT) analysis of benzene – H_2 system

Teobald Kupka[a], Michał Stachów[a], Marzena Nieradka[b], Leszek Stobiński[b,c], Piotr Nowak[d]

[a]*Faculty of Chemistry, University of Opole, 48, Oleska Street, 45-052 Opole*

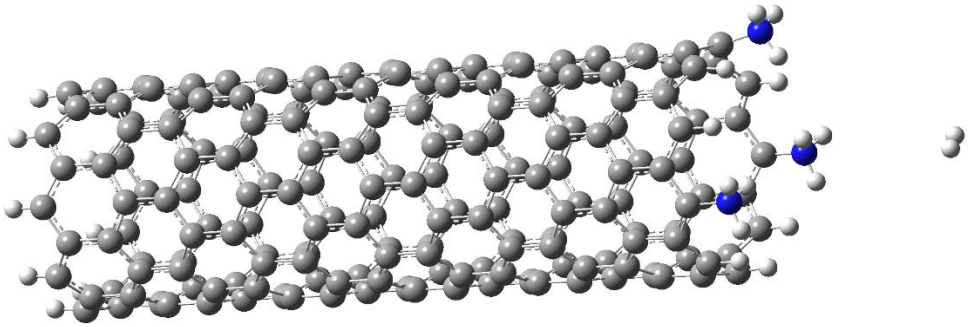
[b]*Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw*

[c]*Faculty of Materials Science and Engineering, Warsaw University of Technology,Wołoska 141, 02-507 Warszawa*

[d]*The Opole University of Technology, Faculty of Electrical Engineering Automatic Control and Informatics, Sosnkowskiego 31 Street, 45-272 Opole*

Applications of single wall carbon nanotubes (SWCNT) and their functionalized derivatives are widely supported by theoretical and spectroscopic studies. Among number of studies are those which aim to understand the nature of weak interactions between small gaseous molecules and the SWCNTs.

In this paper we will discuss the application of specific calculation tools (density functionals), previously selected from detailed studies on rare-gas dimers and benzene – H_2 interactions. The performance of selected density functionals (mPW2PLYPD, B2PLYPD, wB97X, wB97XD, B972), combined with several basis sets will be analyzed and compared to benchmark MP2 and CCSD(T) results.



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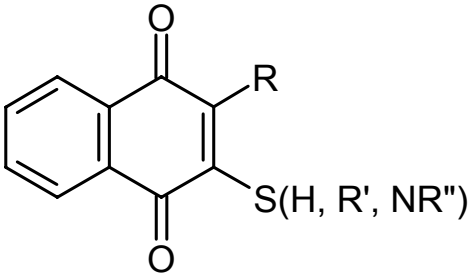
Computer screening-structure-biological activity in the orders of sulfur-containing derivatives of 1,4-naphthoquinone

M. Stasevych, V. Chervetsova, I. Buchkevych, M. Platonov, O. Stanko, R. Musyanovych, V. Novikov

National University "Lviv Polytechnic", Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology, 12 S. Bandera Str., Lviv, 79013, Ukraine; e-mail: vnovikov@polynet.lviv.ua, vladnovikov@list.ru, vladnovikov@ukr.net

Promising direction to realize of the synthesis of new compounds is using a computer prediction of biological activity of compounds with a variety of programs, including *PASS C&T*. When the experimental results match with data of computer prediction is the possibility of using compounds-leaders for the creation of libraries of potential biologically active substances.

A prediction of the spectrum of biological activity of sulfuroderivatives of substituted 1,4-naphthoquinone - thiols, sulfides, sulfenamides by the program *PASS C & T* (Pa>0,5), results of which showed promising research directions of these compounds, particularly for antibacterial, fungicidal, toxic. anticancer, cardiovascular, inflammatory, antimicrobial, acaricidic action, etc., that became the basis for synthesis of new sulfur-containing compounds in the orders of naphthquinonic derivatives and search among them, especially antimicrobial substances.



R = Amino acid, Het; R'=R"=Alk, Ar,Het

Percentages of compounds with predicted antimicrobial and fungicidal action of the 20 compounds studied (Pa>0,5) represented on the diagram (Fig. 1). Experimental microbiological screening showed that some compounds found moderate antibacterial activity, but the substance with high antibacterial and fungicidal activity were discovered.

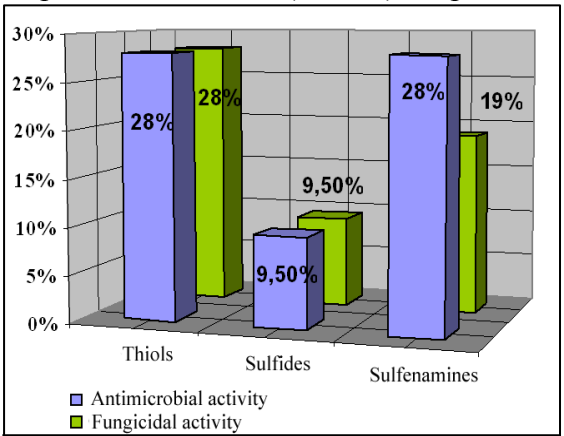


Fig.1. Chart of percentage of compounds with predicted antimicrobial and fungicidal action by PASS (Pa>0,5)

Analysis of theoretically (the program PASS) and experimentally obtained data of antibacterial and fungicidic activity showed that the computer screening of many compounds is confirmed by the experimental biological screening.

Data of antimicrobial activity of compounds allowed to bring correlation "structure - antimicrobial action" and selected perspective compound-leaders among thiols, sulfides and sulfenamides of 1,4-naphthoquinone substituted.

Computational and photoelectron spectroscopy studies on the anionic uridine homodimers

P. Storoniak[a], K.H. Bowen[b], Y.J. Ko[b], H.P. Wang[b], and J. Rak[a]

[a]*Department of Chemistry, University of Gdańsk, J. Sobieskiego 18, 80-952 Gdańsk, Poland*

[b]*Department of Chemistry, Johns Hopkins University, Baltimore, MD 21218, USA*

High vacuum bombardment of dry DNA deposited on a tantalum support with a beam of electrons demonstrated that low energy electrons (LEEs; 0 to 20 eV) were able to induce single and double DNA strand breaks via dissociative electron attachment. Since then the interest in interactions of LEEs with nucleic acid has grown, as it was shown that LEEs are generated in large quantities when living cells are exposed to ionizing radiation. As the experimental and computational gas phase electron affinities suggest, pyrimidine rather than purine nucleobases seem to be most susceptible to electron attack.

In the present study we scrutinize electron attachment to the hydrogen-bonded complex consisting of two uridine molecules – a uridine homodimer. The photoelectron spectrum (PES) for the uridine dimer anions (U_2^-) with the broad signal covering the range 1.4 – 2.6 eV was registered with 2.54 eV photons. The shape of photoelectron spectrum suggests that several low-energy structures are involved in the thermodynamic equilibrium attained under the conditions of the PES experiment.

The B3LYP/6-31++G** level calculations for possible arrangements of U_2^- enabled its five low-energy geometries to be identified. The SOMO distributions for the considered geometries indicate that all anions are of the valence type. These anions differ substantially with VDE and their VDE values fall in the electron binding energy region covered by the registered PES spectrum. We demonstrate strong electron binding by U_2 which may result in the intermolecular proton transfer and the substantial stabilization of the resulting radical anion. Indeed, the most stable anionic species, that has a predominant contribution to the PES signal, is formed from the neutral complex due to electron attachment that is followed by a barrier-free intermolecular proton transfer from the N3H site of one uridine molecule to O8 of the other one on which the excess electron is localized.

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QSAR studies of phosphodiesterase- 4 inhibitors

Vasyl Kovalishyn[a], Vsevolod Tanchuk[a], Larisa Charochkina[a], Volodymyr Prokopenko[a]

[a]Institute of Bioorganic Chemistry & Petroleum Chemistry, National Ukrainian Academy of Sciences, Kyiv-94, 02660, Murmanskaya, 1, Ukraine; e-mail:v_tanchuk@yahoo.com

Phosphodiesterase 4 **(**PDE-4) modulates levels of cAMP regulating several cellular physiological processes, such as leukocyte responses including the proinflammatory actions of monocytes, T cells and neutrophils, airway and vascular smooth muscle constriction, gene transcription through cAMP response elements, protein phosphorylation via cAMP-dependent protein kinase A (PKA), and cyclic nucleotide gated ion channels. Nowadays, PDE-4 has attracted considerable interest because PDE-4 selective inhibitors have potential therapeutic use in a range most of disease - psoriasis, schizophrenia, asthma, osteoporosis, depression, chronic obstructive pulmonary disease and others. The goal of the present study was to create a vast database of PDE-4 inhibitors from different families of compounds and the use of a variety of machine learning techniques for the development of robust QSAR models that could further guide the search for new potent PDE-4 inhibitors.

A wide range of machine learning techniques have been explored, such as Random Forest (RF)[1], Multiple Linear Regression Analysis (MLRA), Associative Neural Network (ASNN), k-Nearest Neighbors (kNN)[2] etc. The models were built with molecular descriptors calculated by Dragon[3] and datasets collected from various sources. The influence of the descriptor set on the model accuracy was evaluated. Descriptors were selected by their importance for Random Forests[1] and by "pruning methods" implemented in ASNN software.[4] The overall best performance was attained by the ASNN and RF methods. The accuracy of all individual models was estimated using 5-fold cross-validation procedures. Obtained Q^2 coefficients were in the range 0.68-074 for regression models and total accuracies Ac=0.84-0.87 for classification models. The consensus QSAR models were also made by integrating the PDE-4 inhibitor activity predicted by all types of models. We have shown that consensus prediction based on the results obtained by all predictive models always provides the most stable decision. The limitations and advantages of the proposed approach are discussed. The method showed to be a potential tool for estimation of new drug-like candidates at early stages of drug development.

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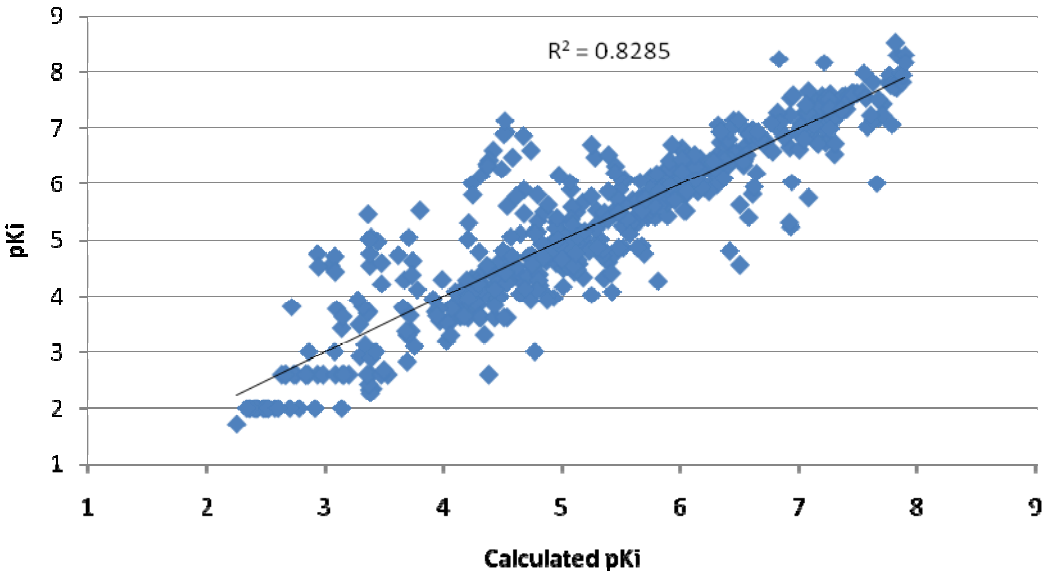
QSAR studies of protein tyrosine phosphatase 1B (PTP1B) inhibitors

Vsevolod Yu. Tanchuk, Volodymyr O. Tanin, Andriy I. Vovk

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, Murmanska, 1, 02660, Kyiv-94, Ukraine; e-mail: v_tanchuk@yahoo.com

Intracellular protein tyrosine phosphatase 1B (PTP1B) is known to be implicated in insulin receptor dephosphorylation and considered a negative regulator of insulin signal transduction. Therefore PTP1B is one of the most promising therapeutic targets for potential treatment of type 2 diabetes and obesity. There is growing interest in developing potent and selective inhibitors of this enzyme.

The goal of this investigation was to create a vast database of chemically diverse PTP1B inhibitors and build a publicly available QSAR model. We have collected 553 compounds from more than 20 sources. The resulting dataset has been uploaded into **Online chemical database with modeling environment (OCHEM)** located at **http://ochem.eu** with a name PTP1B. The dataset is publicly available. A publicly available model is called "PTP1B inhibition(pI), 7124". This is a simple regression model Y = 0.366 + -0.051*ALogPS_logP + -0.093*ALogPS_logS + 0.905*PTP1B inhibition(pI)(PTP1B inhibition(pI), 7069), where ALogPS_logP and ALogPS_logS are LogP and LogS values calculated by ALogPS, PTP1B inhibition(pI)(PTP1B inhibition(pI), 7069) is a prediction by another more complex model (PTP1B inhibition(pI)(PTP1B inhibition(pI), 7069). The later model (7069) has been built using 1902 descriptors calculated by Adriana, EState, ALogPS and Dragon packages. This is an ANN model trained by Supersab algorithm with 1000 iterations, 3 neurons, and 5-fold cross-validation. Parameters of this model are R^2=0.81, q^2=0.81, RMSE=0.69, MAE=0.50. The regression model built upon it (7124) is slightly better with R^2=0.83, q^2=0.83, RMSE=0.64, MAE=0.45.



Computer prediction of biological activity of derivatives of 9,10-antrachinone

O.P. Sabadakh[a] , Je.R. Luchkevych[a], T.M. Taras[a],
O.Z. Komarovska-Porohnjavets[b]

[a]*Prekarpathian National University*

[b]*Lviv Polytechnic National University*

There is always a need in searching new drugs, due to the resistance of different diseases pathogens. The strategy of searching new substances, as potentially bio-active, is defined by accumulated knowledge, about already used substances, about mechanism of their activity and about targets, they have an effect upon. Efficiency of a drug depends on many factors such as the structure of this substance, mechanism of its physiological activity and, what is essential, on its toxicity. Nowadays, the problem of searching of a new bioactive substance can be solved by using specialized computer software that is capable to predict the probability of manifestation of some biological activity, and, on the basis obtained data, to choose the most perspective basic structure. Specialized software system for predicting bio-activity spectrum, Prediction of Activity Spectra for Substance: Complex & Training (PASS C&T), is a convenient tool for predicting bio-activity. It is well known, that biological activity of a substance is the function of its chemical structure. PASS C&T is able to analyze and define the dependence "structure- activity"and predict properties of new substance, by the means of mathematical methods. The results of prediction are presented as a list of activities with corresponding P_a and P_i ordered descending for $(P_a - P_i)>0$. P_a and P_i represent evaluation of the probability for the substance to be active or passive in each case of activity in bio-activity spectrum. If $P_a>0,7$, there is a high probability that substance will show activity in experiments and, also, it is likely that well-known pharmaceutical agents, analogous for this substance exist. If $0,5< P_a<0,7$, than the substance probably will show activity in experiments, but that is not likely, it has known pharmaceutical analogues. And if $P_a<0,5$, that it is unlikely, that the substance will show activity in experiments, but the presence of this activity can be confirmed by the experiments and, probably, this substance will represent new chemical object.

Derivatives of 9,10-antrachinone are widely represented in nature. They are the products of living organisms' life and metabolites of numerous bio-chemical reactions. They are chemical components of many plant cells and often play a basic role in biological activity of numerous medicinal plants.

The results of biological activity predictions show, that anime derivatives of 9, 10-antrachinone with amino-acid fragment and 9, 10-antrachinone derivatives with triazene fragment containing moieties of different nature are interesting for studying them for anti-viral activity, because P_a index, in this correlation, lies between $0,5< P_a<0,7$. They can show anti-protozoan activity; can act as antibiotics with anti-neoplastic properties.

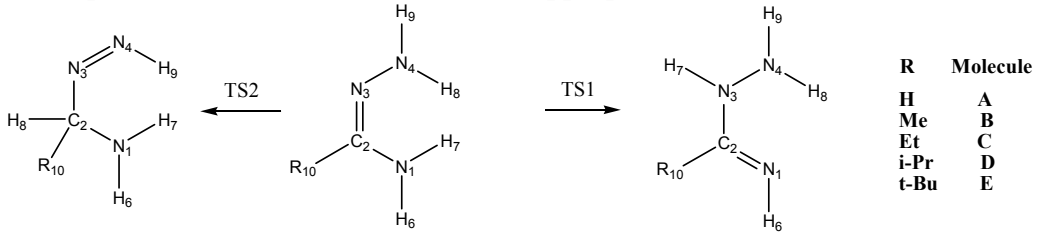
Virtual screening of biological activity lies in good correlation with experimental data, which were obtained as a result of preliminary evaluation of anti-microbial activity against Gramm-negative bacteria Escherichia coli, and Gramm-positive bacteria Staphylococcus aureus, Mycobacterium luteum, using determination of bactericide activity by method of substance diffusion into agar-agar on solid substrate (meat infusion agar). Parallel data were collected in the same manner for Candida tenius and Aspergilus niger (beer-wort agar). Obtained data were compared with the activity data of well-known antibiotics: vankomicine, oxaciline, nistatine. It is evident from experimental data, that the substance, which contains di-phenilamine fragment, shows bactericide activity against Mycobacterium luteum. If one includes tyrosine, tryptophan amino-acids and some aromatic amines into structure of the molecule, it will result in moderate activity against E. coli, S. aureus and A. niger.

Computational study of inter and intramolecular proton transfer in amidrazones

H. Tavakol

Department of Chemistry, University of Zabol, Zabol, Iran; e-mail:hosein_ta@yahoo.com

Amidrazones [1] (or hydrazide imides or amide hydrazones) are the subject of interest by scientists especially because of their capacities in formation of various complexes [2] and their biological activities [3]. The amidrazones are versatile ligands which their complexes were shown antibacterial [4] and antitumor [5] properties. In present research, a complete tautomery scheme and the reaction paths between tautomers for some amidrazones was studied using density functional theory. Moreover, DFT calculations have been used to study of their structural parameters, vibrational modes, solvent effect and kinetic and thermodynamic properties. The amidrazone's skeleton can be presented by three tautomeric form and six isomers. Gaussian 98 program package was employed to calculate molecular parameters, frequencies, solvent effects and kinetic and thermodynamic properties of eight selected hydroxamic acids using B3LYP/6-311++G** level of theory. The absence of imaginary frequencies verified that all structures were true minima. In each pair of tautomers, stationary point geometry with one imaginary frequency has been found and identified as a transition state by applying Schlegel's synchronous-transit-guided quasi-Newton (QST3) method. Furthermore, intrinsic reaction coordinate (IRC) calculations proved that each reaction linked the correct products with reactants. Zero point vibrational energies (ZPVE) and other frequency results were corrected with appropriate scaling factor.



The amidrazone's skeleton can be presented by three tautomeric form and six isomers (above figure). In present work, the structures of isomers and the transition states of five selected amidrazone were optimized and frequency calculations were done on the optimized structures. Then, important molecular parameters, IR frequencies and energetic results were extracted. The relative stabilities of amidrazone isomers in the gas phase are found to be as 1Z >1E >2E >2Z >3E > 3Z >TS(1-2) > TS(1-3). The energy differences between *E* and *Z* isomers are very low and between different tautomers are nearly low, but the energy barriers for tautomerism interconversion at the gas phase are high. The kinetic and thermodynamic data in various solvents (chloroform, tetrahydrofuran, acetone and water) are nearly similar to those in the gas phase but their rates constant are slightly less than those in the gas phase. Moreover, equilibrium and rate constants of tautomerism interconversions in presence of 1-3 molecules of water were calculated. Computed activation barriers show that the barrier energy of water assisted tautomerism is very lower than that in simple tautomerism. Therefore, this water-assisted tautomerism can be performed fast, especially with the assistance of two molecules of water.

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The prediction of acute toxicity and physical-chemical properties on the base of simplex representation of molecular structure

Tinkov O.V.[a], Artemenko A.G.[b], Ognichenko L.N.[b], Polischuk P.G.[b], Kuz'min V.E. [a,b]

[a]*T.G. Shevchenko Transdniestria State University, 107, 25 October street, Tiraspol, MD-3300, Moldova, Transdniestria; e-mail: tinkov84@mail.ru*

[b]*A.V. Bogatsky Physical-Chemical Institute NAS of Ukraine 65080, Lustdorfskaya Doroga 86, Odessa, Ukraine*

Nowadays the environmental pollution is a world-wide problem. Different chemical compounds are the main factor of pollution.

The database «Toxic v.1.1.5.» for acute toxicity and physical-chemical properties of organic substances has been developed. It contains information about 2069 chemical compounds. The «Toxic v.1.1.5.» constitutes a compendium of data extracted from the publicly available scientific literature. Two types of toxicity data are included in the database: acute toxicity and prenatal developmental toxicity. Specific numeric toxicity values such as LD_{50}, LC_{50}, LD_{Lo}, LEL are noted as well as the species studied and route of administration used. The bibliographic source is listed for each citation. The database «Toxic v.1.1.5.» is searchable by chemical name and CAS number. The samples for different conditions have been generated.

The investigation of influence of the molecular structure of different organic compounds on acute toxicity has been carried out by 2D simplex representation of molecular structure with help of approaches Partial Least Squares (PLS). The quite satisfactory QSAR models (R^2=0.81-0.94, Q^2=0.63-0.85, R^2_{test}=0.61-0.84) were obtained. Relative influence of some physical-chemical factors on variation of acute toxicity was estimated on the base of QSAR models.

The physical-chemical properties of compounds are extremely important in pharmaceutical and environmental studies. These properties determine the behavior of organic molecules in the environment as well as their absorption, distribution, metabolism, excretion, and other important properties.

The statistic characteristics of the 2D-QSAR models for the prediction of lipophilicity and aqueous solubility were quite satisfactory (R^2_{oob}=0.79-0.84, R2 test=0.790-0.88).

«Toxic v.1.1.5.» database and developed models are realized as Expert Systems for Ecological Risk Prediction. The authors express sincere graiilude to A.E. Shustikov for fruitful cooperation that made possible the development of this task.

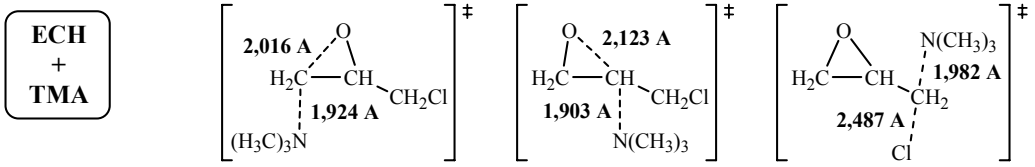
The quantum-chemical investigation of epichlorohydrin-trimethylamine reaction mechanism in vacuo

Tokar A.V., Okovytyy S.I., Renge V.P., Artemoshyna A.A., Kasyan L.I.

Dniepropetrovsk National University named after Oles' Gonchar, 49010, Dniepropetrovsk, 72 Gagarina ave., Ukraine; E-mail: atokar_2004@ukr.net

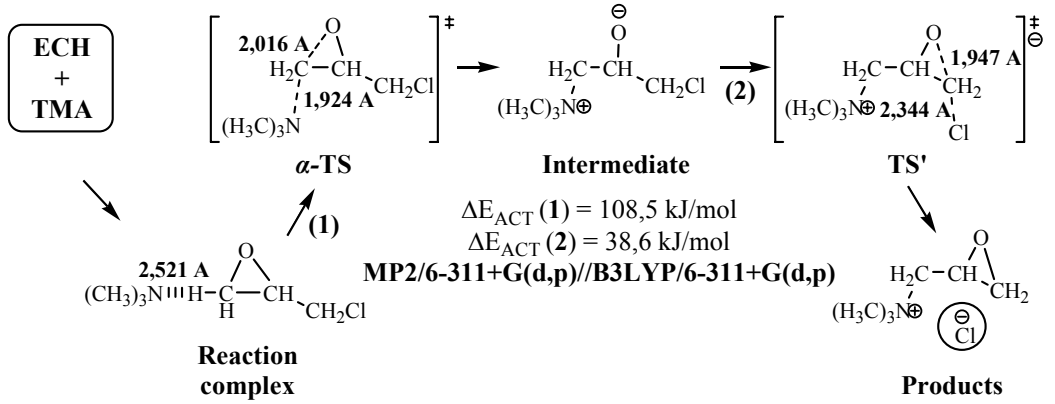
The structure and reactivity of small ring systems continue to fascinate organic chemists. The source of this fascination derives largely from the fact that these compounds offer glimpses into the extremes of bonding in carbon-containing compounds. Of particular interest are heterocycles, the epoxide moiety being one of the principal archetypes. From this point of view the epichlorohydrin (**ECH**) is especial subject for some closer examination [1–4].

The mechanism of **ECH** aminolysis with trimethylamine (**TMA**) *in vacuo* has been investigated at **B3LYP/6-311+G(d,p)** as well as **MP2/6-311+G(d,p)//B3LYP/6-311+G(d,p)** levels of theory. The structures of transition states (**TS**) for three directions of nucleophilic attack are located, and the corresponding values of activation barriers (ΔE_{ACT}) have been evaluated, starting from the point of isolated reagents (**ECH+TMA**).



ΔE_{ACT}, kJ/mol	***α*-TS**	***β*-TS**	***γ*-TS**
B3LYP/6-311+G(d,p)	107,9	151,4	107,5
MP2/6-311+G(d,p)// B3LYP/6-311+G(d,p)	**91,7**	**131,7**	**110,6**

As a matter of fact, the *DFT*-theory does not show any appreciable difference in calculated magnitudes of activation energies, mainly in the cases of α- and γ-nucleophilic attack, whereas the **MP2/6-311+G(d,p)//B3LYP/6-311+G(d,p)** level of theory indicates, that the most preferable direction is the terminal epoxide ring-opening stage. The full reaction route for **ECH-TMA**-interaction is in scheme below.



The results of calculations are in good agreement with that data, which have been obtained for such type reactions formerly [2, 3].

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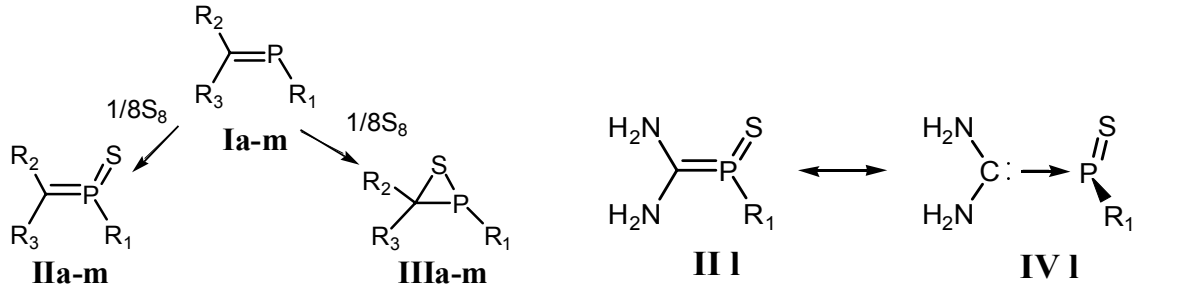
($\sigma^3\lambda^5$)-Phosphoranes vs. ($\sigma^3\lambda^3$)-thiaphosphiranes: quantum chemical calculations of products of phosphaalkene sulfuration

K. V. Turcheniuk[a], A. B. Rozhenko[b]

[a] *Institute of Bioorganic Chemistry and Petrochemistry, Kyiv, Ukraine*

[b] *Institute of Organic Chemistry, Kyiv, Ukraine*

By sulfuration of phosphaalkenes **I** ($\sigma^3\lambda^5$)-phosphoranes **II** or ($\sigma^3\lambda^3$)-thiaphosphiranes **III** are formed [1]. Despite some published experimental data concerning this reaction, the issue remains open, which of structures, **II** or **III** is more preferable in the every concrete case. The process is considered to be thermodynamically driven. In this work the DFT (B3LYP) and coupled cluster (CCSD(T)) calculations of the model and experimental structures of ($\sigma^3\lambda^5$)-phosphoranes **IIa-m** and ($\sigma^3\lambda^3$)-thiaphosphiranes **IIIa-m** have been performed to elucidate the factors influencing relative stabilities of **II** and **III**. The obtained theoretical data allow us to clarify how the process can be managed in order to prepare the products with the desired structure.



I-III: **a**: R_1=Mes*, R_2,R_3= Ph; **b**: R_1=$N(SiMe_3)_2$, R_2=$SiMe_3$, R_3=H; **c**: R_1,R_2,R_3= H; **d**: R_1= F, R_2,R_3=H; **e**: R_1= Cl, R_2,R_3=H; **f**: R_1= SiH_3, R_2,R_3=H; **g**: R_1= NH_2, R_2,R_3=H; **h**: R_1= H, R_2,R_3=F; **i**: R_1= H, R_2,R_3=Cl; **j**: R_1= H, R_2,R_3=SiH_3; **k**: R_1= NH_2, R_2,R_3=SiH_3; **l**: R_1=H, R_2,R_3=NH_2; **m**: R_1=$SiMe_3$, R_2,R_3=$N(SiMe_3)_2$

The results of quantum chemical calculations for **IIa-b** and **IIIa-b** agree well with the known experimental facts: the phosphaalkenes with bulky substituents should be taken as starting materials for preparing ($\sigma^3\lambda^5$)-phosphoranes. However, in addition to the sterical factors, the electronic effects of the substituents R_1-R_3 are also of importance for determining the reaction pathway. In contrast to the currently available experimental facts, in the most cases the cyclic thiaphosphiranes **IIIc-j** seem to be thermodynamically more favored. The only exceptions are the species substituted with the amino and silyl groups. They favor the phosphorane form (**IIk-m**).

Special cases are the bis-amino derivatives **III-m**. They differ considerably from the classic phosphoranes. The main peculiarities of the model structure **II l** are the pyramidal configuration of the phosphorus atom, shortened C-N bonds and noticeably elongated C=P bond. Calculations of frontier molecular orbitals demonstrate that phosphorane **II l** can be alternatively present as a donor/acceptor complex of a stable diaminocarbene with thioxophosphinidene (**IV l**) with the completely separated π systems.

The coupled cluster (CCSD(T)/TZVP) calculations carried out for the small structures provide the geometry parameters very similar to those found at the DFT level of approximation, but the overall stability of **III** seems to be even more pronounced at the more superior level of theory compared to the corresponding isomeric phosphoranes **II**.

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Supramolecular reactions of organic peroxides. Docking of the reactants

N.A. Turovskij[a], E.N. Pasternak[a], E.V. Raksha[a], N.A. Golubitskaja[b]

[a]*Donetsk National University, Donetsk, Ukraine; E-mail: turov@dongu.donetsk.ua*

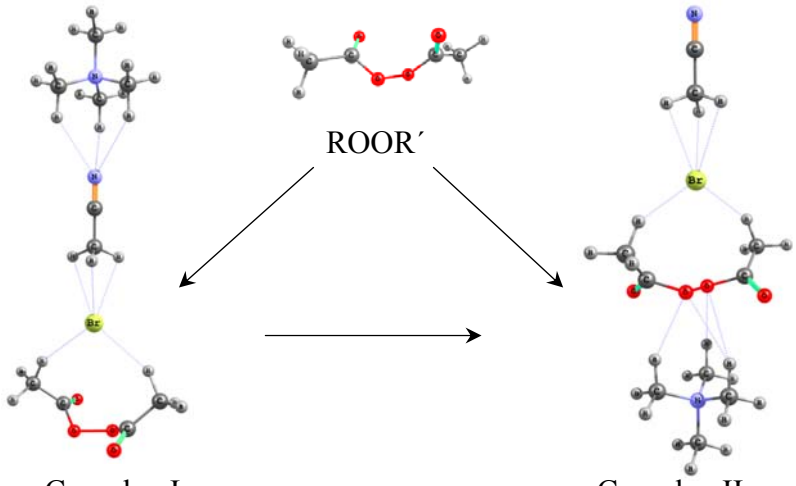
[b]*O.O. Bogomolets National Medical University, Kiev, Ukraine*

Organic peroxides ROOR′ (diacyl peroxides, cyclohexanone peroxides and hydroperoxides, alkyl and aralkylhydroperoxides) generate free radicals in the presence of quaternary onium salts (QX) in mild conditions. Kinetic and NMR-spectroscopic investigations have shown that reaction proceeded through the complex stage. Application of the molecular modelling methods revealed some structural features of the interaction between peroxides and onium salts. All calculations was carried out by semiempirical (AM1, PM6) and DFT-methods.

The first stage of the catalytic peroxide decomposition is the supramolecular complex formation between peroxide molecule and the solvent separated ion pair of the salt (Q^+…Solv…X^-). The main feature of this complex is structural reorganization of the peroxide torsion fragment C-O-O-C that is reaction centre of the system. One can observe the elongation of the peroxide bond O-O and decrease of its strength. Thus selective binding of the reactants occurs on the molecular recognition stage with following chemical activation of the peroxide molecule.

The potential energy surface has been obtained for the supramolecular complex formation. Interaction of peroxides with Q^+…Solv…X^- leads to the formation of two different complexes. In complex I (ROOR′…X^-…Solv…Q^+) the salt anion interacts directly with peroxide and plays the main role in the peroxide bond activation. The salt cation effect is secondary and is realized through the solvent molecule. Complex II is substrate separated ion pair (Solv…X^-…ROOR′…Q^+). In this complex the peroxide molecule is under combined action of the anion and the cation. The complex II has shown to be formed from the structure I [1].

Competition of two observed alternative mechanisms of the peroxides decomposition in the presence of QX is in a good agreement with formation of two different complexes between ROOR′ and QX. The first type interaction of peroxide with QX (complex I is formed) leads to the homolytic O-O bond decomposition and realization of the catalytic mechanism of ROOR′ decomposition. This catalytic scheme has been experimentally observed for the reaction of cyclohexanone peroxides and hydroperoxides as well as alkyl and aralkylhydroperoxides decomposition in the presence of tetraalkyl ammonium halides. When complex II is formed, one can observe the electron transfer from the salt anion onto O-O bond in the transition state of the complex bonded peroxide decomposition. This process leads to the formation of the anion and radical from the peroxide as well as to the partial consumption of the halide anion. This is in a good agreement with experimental features of the diacyl peroxides decomposition that activated by quaternary onium halides.



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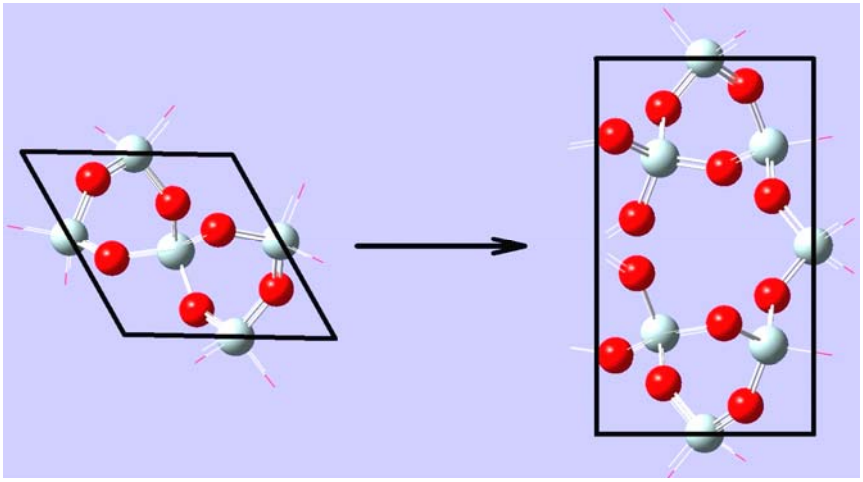
DFT modelling of silver atoms on fully hydrated silica surface (001)

N.I. Vakula[a], G.M. Kuramshina[a]

[a]*Faculty of Chemistry, Moscow State University (M.V.Lomonosov), Moscow, 119991, Russia*

Metal island films (MIFs) have many interesting properties and, particularly, a unique optical behavior. These films are effectively used as selective absorbers, optical polarizers, and data storage, etc. Using the optical behavior of MIFs opens up the possibility to produce low-cost photonic heterostructures.

In the present study, first-principle calculations have been carried out to investigate the electronic structure and adsorption energy of silver atoms deposited on the silica (001) surface. A slab of aquartz, which occurs in $P3_121$ space group, has been set up by using an orthorhombic unit cell.



All calculations have been performed with CP2K code[1]. The technique based on the Quickstep[2] implementation of the density functional theory (DFT) method with Gaussian and plane waves (GPW[3]) scheme has been utilized. We have used the generalized gradient functional PBE and the Goedecker-Teter-Hutter[4] pseudopotentials in conjunction with TZVP basis sets.

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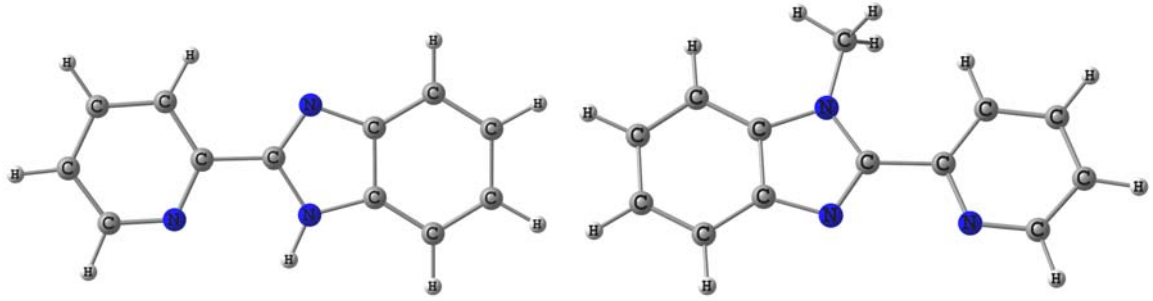
Acknowledgement. We thank Research Computing Center, M.V. Lomonosov Moscow State University for the facilities and the use of SKIF MSU "Chebyshev" Supercomputer. This work was partially supported by the RFBR grant No 011-03-00040a.

Vibrational spectra and DFT calculations of benzimidazole- containing ligands: microhydration and medium influence on vibrational spectra and molecular force fields

O.A. Vakula[a], G.M. Kuramshina[a], D.A. Pichugina[a], V.M. Senyavin[a]

[a]*Faculty of Chemistry, Lomonosov Moscow State University), Moscow, 119991, Russia*

The 2-(2'-Pyridyl)benzimidazole (2PBI) and pyridine belong to the important heterocyclic bioactive molecules. 2PBI is very well known in the coordination chemistry, and in the last time this compound is tested as the parent compound of different aurophilic ligands which form the complexes with transition metal ions and are used for the stabilization of Au nanoparticles. In this study we present results of theoretical investigations of effect of microhydration and aqueous surrounding on the structure and molecular spectra of two ligands, namely, 2-(2'-pyridyl)- benzimidazole **(1),** and 1-methyl-2-pyridin-2-yl-1H-benzimidazole **(2)**:



1 2

Fig. 1. Optimized B3LYP/6-31+G** structures of the most stable conformations of **1** and **2.**

The fully optimized geometries of possible tautomers of **1** and **2** were calculated at the HF and B3LYP levels of theory with 6-31G*and 6-31+G** basis sets. Ab initio and DFT calculations were performed with the program GAUSSIAN 03 (Revision C.02) package [1].

The minima of the potential surface were found by relaxing the geometric parameters with the standard optimization methods. Analytical force constants were derived and harmonic vibrational frequencies were calculated at all investigated theoretical levels.

Relative energies of possible tautomers of **1** and **2** in water solution were also estimated at the B3LYP/6-31+G** level. The influence of solvent environment was considered within the COSMO-RS approach. Harmonic frequencies of the normal vibrations of **1**-**2** were calculated at the same level of theory. Additionally, the associates of **1** and **2** with water molecules were optimized at the B3LYP/6-31+G** level. Trends in changes of structural parameters, vibrational frequencies and molecular force fields under the water surrounding were analyzed. The comparison of theoretical IR and Raman spectra of **1** and **2** in the water surrounding demonstrates strong difference in spectra in all frequency regions with the most evident changes in the positions and intensities of IR bands and Raman lines in the high frequency region.

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Acknowledgement. This work was partially supported by the RFBR grants No 11-03-00040a.

QSPR Analysis of the Mixtures: Modeling of Boiling Temperatures of 2-Component Systems

E. Varlamova[a], I. Oprisiu[b,c], E. Muratov[a,d], A. Artemenko[a], G. Marcou[b], P. Polishchuk[a], V. Kuz'min[a], A. Varnek[b]

[a] *A.V. Bogatsky Physical-Chemical Institute, Odessa, Ukraine*

[b] *University of Strasbourg, Strasbourg, France*

[c] *Processium, 62 Boulevard Niels Bohr - BP 2132 - F - 69603 Villeurbanne, France*

[d] *University of North Carolina, Chapel Hill, USA*

The main goals of our study were application of the SiRMS and ISIDA approaches to QSAR analysis of mixtures of compounds and their benchmarking on boiling temperature of various binary mixtures.

The data set contains 167 mixtures created by different combinations of 67 pure liquids representing totally 3252 data points. Models were developed using non-linear Support Vector Machine (SVM), Associative Neural Networks (ASNN) and Random Forest (RF) approaches. For SVM and ASNN calculations, the ISIDA fragment descriptors were used, whereas Simplex descriptors were employed in RF models. The following tree different strategies of the models validation have been used. (i) "*Points out*": prediction of T_b for any molar ratio of the known biphasic systems. All 67 individual components of the mixtures were always kept in the training set. Mixtures data points were taken to external set. (ii) "*Mixtures out*": prediction of T_b for the missed data in the mixture matrix (gap-filling) formed by 67 pure liquids from the training set. All 67 individual components of the mixtures were always kept in the training set. Whole mixtures were taken to external set. (iii) "*Compounds out"*: prediction of T_b for mixtures created by new pure compound(s) beyond the training set. Both pure liquid and all its mixtures were taken to the external set. N-fold external cross-validation was performed in each strategy. Significant models were obtained having statistical parameters $R^2_{NFECV}>0.79$ and $RMSE_{NFECV}<11.6$ K.

Additional external validation on 96 new mixtures show that the obtained models are well-suitable for gap-filling of the missed data (more than 2000 mixtures) in the mixture matrix formed by 67 pure liquids from the training set, whereas the prediction error for the mixtures formed by new compounds is rather high.

Evolution of Raman Spectra of Pyrimidine Bases under Deuteration

S.G. Garasevich, M.S. Iakhnenko, O.V. Slobodyanyuk, I.V. Vaskivskyi

Department of Physics, Taras Shevchenko National University of Kyiv, 64, Volodymyrska St., 01033 Kyiv, Ukraine; e-mail: igor@vaskivskiy.kiev.ua

Formerly Raman spectra of some pyrimidine bases (i.e. cytosine, uracil) and their deuterated analogs were measured [1]. It was revealed that some Raman peaks experience low frequency shifts under deuteration (commonly known isotopic effect). But at the same time, some other peaks experience apparent high frequency shifts [2]. To reveal the reasons of such unexpected high frequency shifts the computer calculation of Raman spectra were made using Gaussian 03 package with DFT/b3lyp level of theory and 6-31+G (d,p) basis set [3,4].

Experimentally the mass of hydrogen atoms in certain organic molecule can be changed only discretely with step 1 from 1 a.u. to 2 a. u. (deuterium) and to 3 (tritium) i.e. magnitude of possible step is comparable with absolute value of mass. So observed Raman spectra undergo considerable changes not only in absolute value of Raman shifts of peaks but also considerable changes in their intensities. Therefore it is difficult to match corresponding Raman peaks of deuterated and non-deuterated sample. But using quantum-chemistry calculations it is possible to model spectra of molecules that contains hypothetic isotopes of hydrogen with mass that changes smoothly. It makes possibility to trace the evolution of spectra under deuteration.

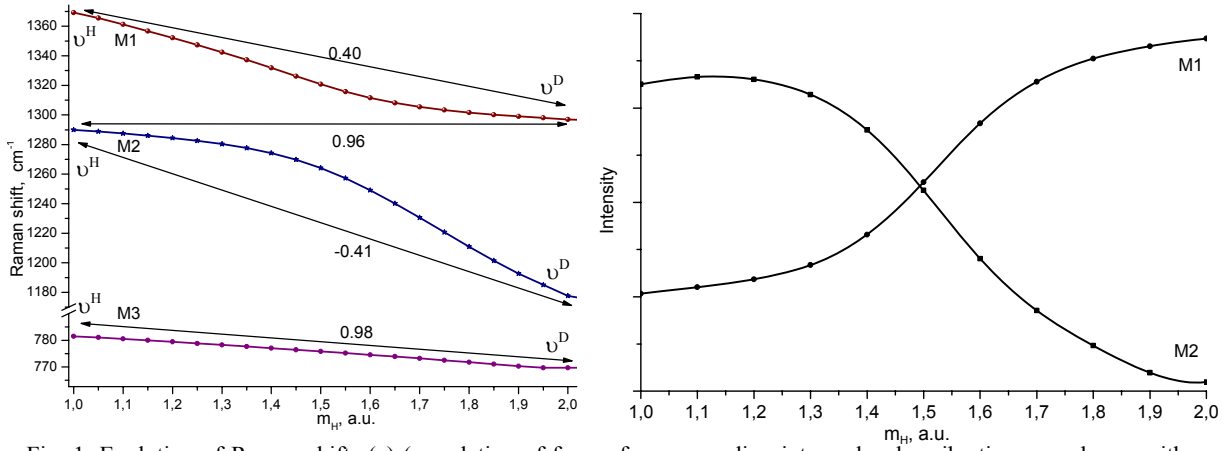

Fig. 1. Evolution of Raman shifts (a) (correlation of form of corresponding intramolecular vibrations are shown with arrows) and intensities (b) of two adjacent Raman modes of cytosine molecule under deuteration.

As the result of such calculations, we could conclude that all high frequency shifts in Raman spectra under deuteration are only apparent and not connected with increasing of eigenfrequencies of molecule but caused by redistribution of intensities of adjacent modes. Such redistribution is a result of changes in form of intramolecular vibrations.

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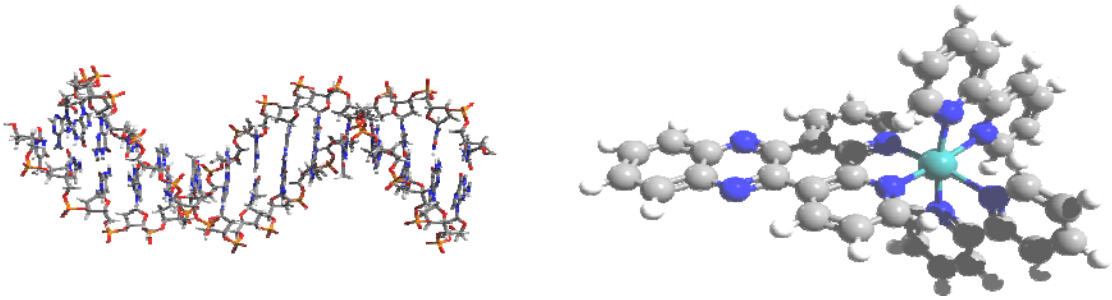
[4] S.Garasevych, M.Iakhnenko, O.Slobodyanyuk, I.Vaskivskyi XXII International Conference of Raman Spectroscopy, AIP Conference Proceedings, p.664, (2010)

UV-VISIBLE spectra of ruthenium complexes in interaction with DNA

Thibaut Very, Xavier Assfeld

Équipe de Chimie et Biochimie Théoriques (CBT), UMR 7565 CNRS-UHP, Institut Jean Barriol (FR CNRS 2843), Faculté des Sciences et Techniques, BP 70239, Boulevard des Aiguillettes, 54506 Vandoeuvre-lès-Nancy, France



Transition metal complexes are widely used and the coverage of applications is quite broad. In medicine domain, and particularly concerning treatments of diseases like cancer, platinum complex known as cisplatin is given daily. However, the side effects felt while taking this drug are strong. In order to reduce side effects, research has turned toward other transition metal, showing less cytotoxicity, like ruthenium.[1] Combined with polypyridyl ligands, it show interesting photoluminescence properties and can be used as a light probe of the interaction with DNA.

Here we present a combined QM:MM study of the interaction between DNA and a ruthenium complex : [dipyridophenazino,bisbipyridino,ruthenium]$^{2+}$. This complex exhibit fluorescence while interacting with DNA whereas this fluorescence is quenched in aqueous media.[2] Firstly, we carried out MM minimizations on a system made of a 15 base pairs B-DNA, the complex intercalated into the double strand and a cylinder of water molecules, in order to see which configurations are more likely to happen. These calculations are being followed by QM:MM optimizations and finally TDDFT calculations to retrieve UV-Visible absorption spectra. We show the effect of intercalation into DNA for the complex.

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The use of modern operating amplifiers for electrophysiology researches

[a]H. Yaremkevych, [b]Y. Tolopko, [a]O. Skorokhoda, [a]V. Novikov

[a]Lviv National Polytechnic University 12, S. Bandera St., Lviv 79013, Ukraine; e-mail: yaremkevych.os@gmail.com

[b]G.B. Karpenko Phisical-Mecanical Institute, NAS of Ukraine 5, Naukova St., Lviv 79601, Ukraine

A study of electric potentials has great importance both for understanding of nature of these processes and for the display of character of violation of the activity of living cells at different types of pathology. The method of microelectrode technique is used in biophysics for the study of the biological diaphragm phenomena. Since a cell membrane in the state of rest is polarized - an external surface has positive charge, and internal – negative charge, there is a potential difference of about (-60÷-90 mV) between its external and internal surfaces, which can be registered by microelectrodes, connected to a cell and a measuring device. The study of electric properties of membranes of separate cells gives important information about the mechanisms of action of pharmacological agents and physiologically active substances and allows to trace the changes of electric properties of cells. The embryos of loach *Misgurnus fossilis* L. were used in the research. A signal which arose up on the polarized cell was fed to the input of the amplifier and anplified in 20 times. Then a signal from the amplifier output was fed to the input of analog-to-digital converter (ADC), and the converted data were displayed on the monitor of personal computer in form of charts of two temporal involutes and simultaneously written into a text file by the specialized software. The indices of diaphragm potential were registered on this installation continuously during 5-6 hours of the development of embryos.

For the diminishment of the influence of the amplifier input resistance on the result of measurement an operating amplifier (OA) was applied with the field-effect transistors on its input - monolithic OA of OPA128 type. A special geometry of the dielectrically isolated field-effect transistors is used in this OA, which provides higher parameters than in the previously known hybrid operating amplifiers. It allows to support very low bias current – $75 \cdot 10^{-15}$ A, low bias voltage – 500 μV but, at the same time, low bias voltage drift – 5 μV/°C. It enabled the increase of sensitivity of the measured signals. The amplifier input resistance for a differential signal was 10^{13} Ohm, and for a cophased signal - 10^{15} Ohm. Input capacity was below 1 pF. Maximum frequency at an amplification factor 1 was1 MHz.

A signal from the amplifier output was fed to the ADC input. ADC with the serial data output was chosen. Such ADC is characterized with insignificant consumption and small sizes. It allows to build compact ADC with the minimum number of external connections. In this case the ADC of MAX1243 type manufactured by MAXIM Company was used. It is ten-bit ADC which provides the transformation error not greater than 0,3% (relative error, differential non-linearity, bias error, internal amplifier error).

It is necessary to study the biopotentials that change in a range ±100 mV. At the biopotential amplification coefficient of 20, the voltage on the ADC input will change in a range ±2 V. This ADC can convert input voltage from 0 to positive optimum voltage. For work with an input signal in a range ±2 V the potential bias of input socket on +2 V should be applied and the reference voltage +4V should be chosen. The ADC is connected to the computer through serial port. Signals from ADC to the computer and from a computer to ADC passed through photocouplers, which diminish the influence of computer work on biopotential amplifier work.

The software program for "Windows" operating system was developed for reading and analysis of data from ADC. The developed software program executes three functions – reads the signal from serial port with a given time interval, writes these data into a file on a hard drive and displays a graphic dependence of the signal (potential value) from time in form of two charts (the first one reveals the dependence in the given time interval, the second one – dependence during all experiment). The data from the obtained file in form of pairs "time – potential value" will enable further disclosure of the dependence between these indices.

The role of intermolecular hydrogen bonds in specific binding of stavudine triphosphate to HIV-reverse transcriptase active site

A. G. Ponomareva, Y.P. Yurenko, D.M. Hovorun

Department of Molecular and Quantum Biophysics, Institute of Molecular Biology and Genetics, NAS of Ukraine, 150 Zabolotny Str., Kiev - 143, 03143, Ukraine

The present work aims to understand molecular mechanisms of biological activity of stavudine (3'-didehydro-2'-3'-dideoxythymidine, d4T), a nucleodide analogue reverse transcriptase inhibitor. To achieve this purpose, we resorted to hybrid quantum mechanical/molecular mechanical (QM/MM) modeling of d4T triphosphate (d4TTP) in the HIV-1 reverse transcriptase active site. The similar simulations were also performed for canonical nucleoside thymidine triphosphate (dTTP). X-ray crystal structure of the catalytic HIV1-RT/DNA/dTTP complex (pdb ID 1RTD) was taken for investigation *in silico*. Two sets of QM/MM calculations (one with d4TTP in the nucleotide binding site and the other with dTTP) were carried out. Minimized solvated and neutralized molecular systems were subject to canonical ensemble (NVT) molecular dynamic simulation lasting 100 ps with the Amber99SB-ILDN force field. In the latter case position restraints were imposed on the atoms of HIV1-RT/DNA/dTTP complex to equilibrate solvent molecules. The output systems were used for further QM/MM investigation. QM calculations were performed using B3LYP/3-21G/6-31G* method. Hydrogen bonds (H) were identified by means of geometrical criteria.

Both d4TTP and dTTP in the binding site of the HIV-RT form various types of H-bonds with amino acid residues as well as with the surrounding water molecules. The former H-bonds are mainly of NH···O type, where NH group of an amino acid interacts with oxygen atoms (O) located in nucleoside triphosphates. This lace of the H-bonds facilitates the Pα-Oα3 bond dissociation, dramatically enhancing the HIV-RT polymerization activity. The intramolecular O3'H···Oβ1 H-bond, which is formed between dTTP and HIV-RT, deserves a special attention. It can be inferred that the lack of the O3'H hydroxyl group in d4TTP and therefore of the O3'H···Oβ1 bond inhibits its incorporation into DNA nascent chain in comparison with its natural analogue. It should be also noted that H-bonds between nucleotide triphosphate group and positively charged tail of Lys65 play an important role in the binding process, since replacement of Lys65 to Arg residue (K65R) causes resistance to some nucleoside analogues, devoid of the O3'H group.

Quantum chemical modelling of interionic interactions in carboxylic acid cation exchangers on the base of polyacrylic acid

V.M. Zelenkovskii, T.V. Bezyazychnaya, V.S. Soldatov

Institute of Physical Organic Chemistry Belarus National Academy of Sciences, 13, Surganov St., Minsk 220072, Belarus; e-mail vmzel@ifoch.bas-net.by

Ab initio calculations of the structure of representative fragments of carboxylic acid cation exchangers on the base of polyacrylic acid in forms of alkali, alkali earth and some heavy metal ions (Cu^{2+}, Ni^{2+}, Cd^{2+}, Mn^{2+}, Pb^{2+}) have been done by method RHF SCF MO LCAO. In the case Ni^{2+} and Cu^{2+} in the main valence state the calculations were done by ROHF SCF MO LCAO method. For calculations of local interionic and intermolecular interactions the program FIREFLY [1] was used. For large multiatomic systems the best results gave non-empirical calculations with minimal basis set Huzinaga MINI [2]. Some properties of sorption complexes are calculated with using of HF/6-31G(3d) and B3LYP1/6-31G(3d) level of the theory. The calculated fragments contained up to twelve repeating units of the polymer chain, the counterions and 0 – 10 water molecules per carboxylate group. The geometry and electronic characteristics of Me – O bonds with carboxylic groups and water molecules in the hydration systems were analyzed. The ionic hydration in these systems was characterized by the number of water molecules directly bound only to the carboxylic groups, only to the counterion both to the carboxylate group and the counterion, only to the other water molecules. It appeared that in all cases the counterions are strongly bound with carboxylate groups forming rigid structures in which one univalent counterion can be directly bound to two carboxylate groups. The bivalent cations are mainly bound to three carboxylate groups. The electro neutrality of the polymer fragment is provided through the group binding of the counterion and the carboxylic groups. The significant degree of covalence of the bonds between the cations and carboxylic group dependent on the atomic mass and number of water molecules in the system is mainly responsible for the selectivity series of the alkali and alkali earth metals. These series are opposite to those for sulfonic cation exchangers. The high selectivity of sorption of the heavy metal ions is due to the fact that Me–O bonds with oxygen atoms of both carboxylate groups and water molecules have high degree of covalence. These interactions are competitive and their balance is individual for any pair of fixed and counterion.

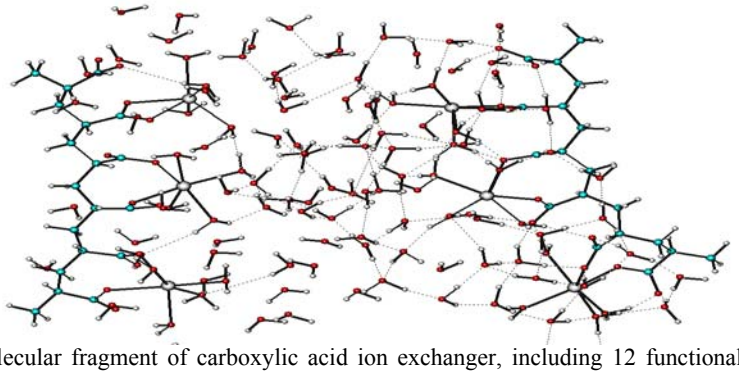

Figure. Structure of molecular fragment of carboxylic acid ion exchanger, including 12 functional groups and 120 water molecules.

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Towards estimation of stacking interaction energy from electron density distribution

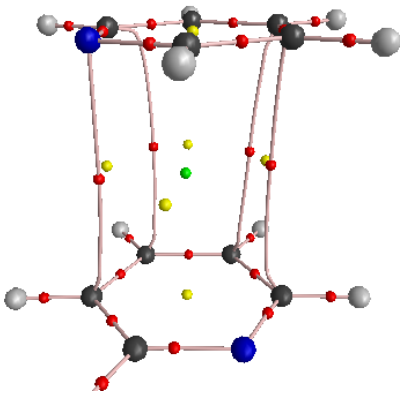
Oleg A. Zhikol, Oleg V. Shishkin

STC "Institute for Single Crystals" NAS of Ukraine, 60 Lenina ave., Kharkiv, Ukraine; e-mail: zhikol@xray.isc.kharkov.com

Stacking interaction, defined as an attractive interaction of two parallel π-conjugated systems, was noticed at first in the DNA bases packing, but later was recognized as a common interaction pattern, inherent also to peptides and to great many conjugated cyclical structures packed in the crystal. It is caused mainly by Van der Waals forces, more specifically, induction and dispersion. From the viewpoint of applied quantum chemistry, these phenomena are dominated by electron correlation effects. This fact substantially complicates evaluation of the stacking interaction energy.

On the basis of R. Bader's "Atoms in Molecules" (AIM) theory [1], nearly ten years ago a simple formulae was proposed for the estimation of hydrogen bond energy [2]. Since then it was applied to many weak atom-atom interactions outside of initial purpose and showed promising results.

Extending our previous results for benzene dimer [3], we supplement model structures with stacked dimer of pyridine molecules. The full set contains 300 structures; BSSE corrected interaction energy in a dimer was computed at MP2(FC)/6-31+G(2d,2p) level of theory (see [3] for details). The Espinosa's formulae [2] gives unacceptable results even for attractive regions of PES. Its failure may be attributed to a complex intermolecular bond topology, see Figure for an example. Surprisingly enough, our previous equation [3] fitted to benzene dimer describes pyridine dimer virtually not worse.



We considered seven parameters of the bond, ring, and cage critical points (CP) of electron density field found between molecules in a dimer. From these, energetic values (kinetic, G, and potential, V, energy density, along with electron density Laplacian) suit the best way the (multi)linear empirical correlation equation. It turned out that the independent variables group as (V-G) within error bounds for each of the three CP types. This lowers twice the number of independent variables, but leads to decrease of regression multiple-R^2 value from 0.971 to 0.541. Including the Laplacian into independent variables set improves this value to 0.958. However the quality of the regression is not acceptable still because the largest absolute error attains 6 kcal/mol for points of PES with strong (>15 kcal/mol) repulsion. Mean square error of the fit is 1.6 kcal/mol, which is too high also. The results can be improved with using values from each individual CP rather than average per CP type ones, thus weighting the CPs dependently on the "interaction graph".

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Computational Studies of a Series of 2-Aminopyrimidin-4(3*H*)-ones as Potent HIV-1 Reverse Transcriptase Inhibitors by Using of Continuous Molecular Fields

I. I. Baskin [a,b], P. V. Carpov [a], N. I. Zhokhova [a], M. B. Nawrozkij [c], A. N. Zefirov [a], A. S. Yablokov [c]

[a] ***Department of Chemistry, Moscow State University, Moscow, Russia***

[b] ***Laboratoire d'infochemie, UMR 7177 CNRS, Université de Strasbourg, France***

[c] ***Volgograd State Technical University, Volgograd, Russia***

Non-nucleoside reverse transcriptase inhibitors (NNRTI) constitute a promising class of organic compounds for developing anti-AIDS drugs. The complex nature of physiochemical interactions between inhibitors of this type and the enzyme binding site was studied using the novel Method of Continuous Molecular Fields (MCMF), suggested by us earlier [1], which describes molecules by means of continuous electrostatic, steric, hydrophobic and other fields (encapsulated into kernels) reflecting different types of intermolecular interactions. Such description is possible with the conjunction with the support vector machine (SVM) method. Parameters of regression (SVR) models obtained for inhibiting activity of structural analogs of 2-Aminopyrimidin-4(3*H*)-ones, lg(EC_{50}) against reverse transcriptase of HIV-1 wild and 3 mutant strains are presented in the Table:

Strain	**Database**	**Kernels**	q^2	**RMSE**
Wild type	1045	Electrostatic, hydrophobic	0,53	0,69
K103N	330	Steric	0,61	0,51
Y188L	330	Electrostatic, hydrophobic	0,56	0,53
IRLL98	128	Electrostatic, abrahams	0,51	0,7

Any QSAR model is used within its applicability domain which could be determined by the one-class classification method [2-3]. The basic scheme for virtual screening workflow enables at the first step the estimation of the applicability domain for a test compound. If the test succeeds at the second step EC_{50} value is calculated prioritizing screened structures. The performance of the one-class classification model is evaluated by the area under the ROC-curve. In this study we used HIVRT decoys subset from the DUD database[4] as inactive compounds to perform the ROC-analysis. The performance of one-class models resulted in AUC > 0,95 for all models built.

Combining classical QSAR models with the estimation of applicability domain allows to create a powerful filter for virtual screening due to boosting the first model by the second one.

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Computer modeling of molecular aggregation in liotropyc liquid crystal

Valery Pogorelov, Iurii Zhovtobriukh

[a]Physical Faculty, Kiev National Taras Shevchenko University, Glushkova str. 2, building 1, Kiev 03022.

As known, the one of the most interest of liotropic liquid crystals are chromonic liquid crystals. Chromonic liquid crystals are formed in solutions of large plane molecules and have columnar structure. Chromonic mesophase are usually formed in solutions of dyes and some medicinal substances. Commonly, molecules of chromonic liquids crystals have a planklike or disklike polyaromatic central core with polar group at the periphery. In water or other solvent, the molecules stack on top on each other forming the molecular aggregates. These molecular aggregates are the structure units of chromonic liquids crystals mesophases. So the properties of liquid crystals mesophases must depend on the molecular and geometric parameters of molecular aggregates which are formed these phases.

In this work the computer quantum-chemical simulation of disodium chromoglycate (DSCG) was performed. Computer simulation consists of computation of equilibrium geometry, total energy and molecular parameters of single DSCG molecule. Then it was computed the energy and equilibrium structure of simplest supramolecular structure such as the DSCG dimer. Computations were performed by the program package “Gaussian-03” using the DFT theory with potential B3LYP. Computations were performed including different basis sets for obtaining most reliable results. Obtained computational data were compared with experimental spectroscopic data.

Intermolecular interactions in the crystal structure of benzene-acetylene co-crystal

Roman I. Zubatyuk, Oleg V. Shishkin

STC "Institute for Single Crystals" NAS of Ukraine, 60 Lenina ave., Kharkiv, Ukraine; e-mail: roman@xray.isc.kharkov.com

Energetic analysis of intermolecular interactions in molecular crystals provides a unique information closely connected to physical and chemical properties of a crystal, such as mechanical properties, preferred morphology, solubility, and also very useful in crystal engendering. Usually, the analysis is performed by establishing (based on geometrical parameters) main strong specific interactions forming supramolecular synthon and minor weak interactions gluing these synthons together. However, in the case of absence of such strong interactions the qualitative analysis becomes ambiguous. From this point the benzene-acetylene co-crystal is being interesting because only weak intermolecular interactions were found in crystal.

Crystal structure of benzene-acetylene co-crystal was obtained from Cambridge Crystal Structure Database (refcode ELIQIZ). Positions of hydrogen were normalized according to quantum-chemical data. The structure has $R\bar{3}$ space group symmetry, Z=3, Z'=$^1/_{12}$, both benzene and acetylene molecules are in special position. Analysis of molecular Dirichlet polyhedrons shows that the first coordination sphere of benzene molecule includes 6 benzene molecules and 8 acetylene molecules. First coordination sphere of acetylene molecule contains 8 benzene molecules. Considering crystal symmetry, there are three unique intermolecular interactions of central molecule with its neighbors: benzene-benzene parallel-displaced stacking, and two types of C-H...π between benzene and acetylene molecules in which π-system of either benzene or acetylene is a proton acceptor.

Quantum-chemical calculations at MP2, LPNO-CEPA/1 and CCSD(T) levels of theory extrapolated to complete basis set shows that the C-H...π(benzene) hydrogen bond in the crystal (-2.7 kcal mol^{-1}). Stacking interactions are weaker (-2.0 kcal mol^{-1}) due to very large parallel shift of the molecules of 4.9 Å. C-H...π(acetylene) even weaker (-1.0 kcal mol^{-1}). MP2 method systematically overestimate interaction energies by about 20%, compared to CCSD(T). LPNO-CEPA/1 method, which has excellent performance (calculations are feasible up to about 2000 MOs) and usually slightly better that CCSD, gives errors on interaction energies of about 0.1 kcal mol^{-1} (less than 10%). Among DFT methods, B3LYP-D3 has the best performance for intermolecular interaction energies within benzene-acetylene crystal (errors are less than 10%). Analysis of electron density distribution in a molecular cluster containing benzene molecule and its first coordination sphere confirms that Dirichlet polyhedrons method gives the correct set of closely interacting molecules. Energetic analysis of a crystal packing demonstrates that the main supramolecular synthon formed due to C-H...π(benzene) hydrogen bonds, the interaction energy within the chain is 2.7 kcal mol^{-1}. Each chain interacts with 6 equivalent neighboring parallel chains, the interaction between chains is 1.9 kcal mol^{-1}.

Interdisciplinary Nanotoxicity Center - JSU

Nanoscience and nanotechnology are one of the fastest growing research and industrial areas in the 21st Century. Nanotechnology has gained a great deal of public interest due to the needs and applications of nanomaterials in almost all areas of human endeavors including industry, agriculture, business, medicine and public health. Nanoscience provides basic information on the species of potential commercial applications. Both nanoscience and nanotechnology rank among the most prominent and rapidly emerging fields that have provided opportunities to individuals with various academic backgrounds (chemists, biologists, physicists, material scientists, engineers, medical specialists and toxicologists) and scientific expertise to understand and manufacture nanoscale objects. One of the issues that have to be addressed in the near future, before massive fabrication of nanomaterials, is their toxicity to humans and the environment.

While there have been significant advances in nanoscience and nanotechnology, there have been concerns that the wide production and utilization of nanomaterials is rapidly overtaking efforts to evaluate their toxicity to humans and the environment. To date, very few studies have focused on the evaluation of the impact of nanomaterials on human health. Limited toxicological data indicate that nanomaterials exposure poses a potential risk to biological systems. In-vitro studies with human skin cells and lung epithelial cells have reported that exposure to single wall carbon nanotubes induces oxidative stress and apoptosis. Very limited data are available on the absorption and toxicokinetics of nanomaterials, as well as on their fate and transport in the environment. As their industrial production increases and the products containing nanomaterials build up in the environment, the potential risk of adverse effects is also expected to increase significantly.

Other areas of concern are the lack of appropriate test models, test protocols, and biomarkers of exposure, sensitivity and effects associated with human exposure to nanomaterials. Also unknown are the most effective ways of protecting workers and/or regulating the production, use and disposal of nanomaterials. Taken together, there exists a big gap in scientific data regarding the toxicology, risk assessment and management of nanomaterials.

Therefore, we enhanced the research capabilities of the Jackson State University by the establishment of the Nanotoxicity CREST Center that efficiently integrates experimental and computational research with undergraduate and graduate education and training of minority students. The Center develops new approaches to enhance knowledge related to nanomaterials, their practical applications and environmental effects and implement an integrated education and research program in the area of nanotoxicity It is anticipated that the implementation of the above-stated studies would provide new insights into the mechanisms of the toxic action of nanomaterials, as well as relevant scientific information for making informed decisions regarding the cost-effective management of nanomaterials. The Center also provides an excellent opportunity to train undergraduate and graduate students in the emerging area of nanotoxicology. Both undergraduate and graduate (Ph.D.) students are welcome in the Center. Successful candidates should have strong background in applied quantum-chemistry and in depth training in physical, organic, inorganic chemistry and math and desire to apply it to the solutions of chemical and biological and material science problems. If you are interested please contact during the Conference Drs. Leonid Gorb or Jerzy Leszczynski or send your curriculum vitae to lgorb@icnanotox.org or jerzy@icnanotox.org.

Virtual Organization CompuChemGridUA: Grid Resource Provider for Computational Chemistry

Computational cluster at the STC "Institute for Single Crystals" NAS of Ukraine is one of the oldest in Ukraine. For many years it has been used by researchers from the Institute for Single Crystals and a number of other academic institutions of Ukraine. In 2003 Ukrainian-American Laboratory of Computational Chemistry (UALCC) was established, which provided access to computational cluster for scientific groups from more than 15 academic institutions and universities. In 2010 the cluster was expanded by joining with the computational cluster of Institute for Scintillation Materials NAS of Ukraine and also integrated to Ukrainian national grid infrastructure, which is compatible with European Grid Infrastructure (EGI). In order to provide access to the computational resources for scientists working in the field of computational chemistry, the virtual organization CompuChemGridUA was established. Our main goal is to combine our experience in support of computational projects through UALCC with the benefits of using grid infrastructure.

The advantages of being a member of CompuChemGridUA are:

- access to computational cluster at STC "Institute for Single Crystals" and to other similar systems in Ukraine and Europe
- technical support for use for grid infrastructure for your computational project

We invite Ukrainian and European researchers to join CompuChemGridUA.

For more details about current CompuChemGridUA terms and project look at our web page at

http://compuchemgridua.org

Contacts

VO manager: Prof. Oleg V. Shishkin, e-mail: shishkin@xray.isc.kharkov.com
VO administrator: Roman I. Zubatyuk, e-mail: roman@xray.isc.kharkov.com