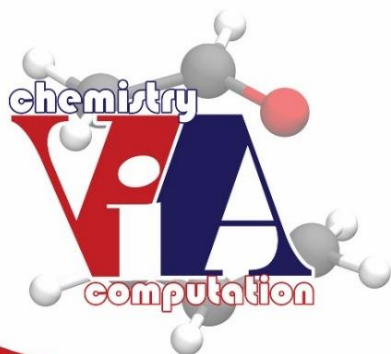




International  
Symposium on

**Chemistry V&A Computation**  
**Applications on Molecular Nanoscience**

**2017**  
**OCTOBER, 30**  
**Istanbul,**  
**Turkey**

**ABSTRACT BOOK**

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INTERNATIONAL SYMPOSIUM ON  
CHEMISTRY ViA COMPUTATION  
APPLICATIONS ON MOLECULAR  
NANOSCIENCE

OCTOBER 30, 2017  
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CHEMViACOMP Özet Kitabı Boğaziçi Üniversitesi Matbaası tarafından  
basılmıştır.

*This symposium is dedicated to Prof. Viktorya Aviyente  
on the occasion of her 40 years in science.*



CHEMViACOMP Organizasyon Komitesi olarak katkılarından dolayı Boğaziçi Üniversitesi Rektörlüğü'ne teşekkür ediyoruz.



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# SYMPOSIUM PROGRAM

|                  |                                                                                                                                                          |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| 08:45-09:30      | Registration                                                                                                                                             |
| 09:30-09.45      | Opening Remarks                                                                                                                                          |
|                  | <b>Session I</b>                                                                                                                                         |
| 09:50-10:35      | Prof. Gerald Monard, France<br>Molecular modeling of the reaction of deamidation in peptides and proteins using combined approaches                      |
| 10:35-10:55      | Assist. Prof. Bülent Balta, Turkey<br>GTP hydrolysis in the elongation factor EF-Tu                                                                      |
| 10:55-11.15      | Dr. İlke Uğur, Turkey<br>1,3-Dipolar cycloaddition reactions of low-valent rhodium and iridium complexes with aryl nitrile N-oxides                      |
| 11:15-11:30      | Coffee Break                                                                                                                                             |
|                  | <b>Session II</b>                                                                                                                                        |
| 11:30-12:15      | Prof. Paul Geerlings, Belgium<br>From conceptual density functional theory to molecular electronics                                                      |
| 12:15-12:35      | Prof. Sondan Durukanoglu, Turkey<br>Molecular motion on metal surfaces: Quantum and classical mechanical approaches                                      |
| 12:35-12.55      | Assoc. Prof. Hande Toffoli, Turkey<br>A comparative study of the polymer-nanotube interface through a reactive force field and density functional theory |
| 12:55-14:15      | Lunch Break                                                                                                                                              |
|                  | <b>Session III</b>                                                                                                                                       |
| 14:15-15:00      | Prof. Michael Feig, USA<br>Molecular dynamics simulations of biomolecules: Facing the challenges in connecting with biology                              |
| 15:00-15:20      | Prof. Canan Atılğan, Turkey<br>Deciphering equilibrium and kinetic properties of iron transport proteins by computational means                          |
| 15:20-16:05      | Prof. Maria Ramos, Portugal<br>Predicting catalytic mechanisms of enzymatic reactions                                                                    |
| 16:05-16:25<br>4 | Prof. Nilsun İnce, Turkey<br>A Bridge between Computational Chemistry and                                                                                |

|             |                                                                                                |
|-------------|------------------------------------------------------------------------------------------------|
|             | Environmental Science                                                                          |
| 16:25-16:40 | Coffee Break                                                                                   |
|             | <b>Session IV</b>                                                                              |
| 16:40-17:25 | Prof. Viktorya Aviyente, Turkey<br>What have we learned with computational tools in chemistry? |
| 17:25-17:50 | Video Presentation                                                                             |
| 17:50-18:00 | Closing Remarks                                                                                |
| 18:00-19:15 | <b>Poster Session</b>                                                                          |
| 18:00-18:45 | Roundtable meeting on “Applications on Molecular Nanoscience”                                  |



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# INVITED LECTURES

*(Alphabetical order according to the last name)*

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# **I1-Deciphering equilibrium and kinetic properties of iron transport proteins by computational means**

Canan Atılgan

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With the advances in three-dimensional structure determination techniques, high quality structures of iron transport proteins transferrin and the bacterial ferric binding protein (FbpA) have been deposited in the past decade. These are proteins of relatively large size, and developments in hardware and software have only recently made it possible to study their dynamics on standard computational resources. We discuss computational techniques towards understanding the equilibrium and kinetic properties of iron transport proteins under different environmental conditions. At the detail that requires quantum chemical treatments, the octahedral geometry around iron has been scrutinized and that the iron coordinating tyrosines are in an unusual deprotonated state has been established. At the atomistic detail, both the N-lobe and the full bilobal structure of transferrin have been studied under varying conditions of pH, ionic strength and binding of other metal ions by molecular dynamics (MD) simulations. These studies have allowed answering questions, among others, on the function of second shell residues in iron release, the role of synergistic anions on preparing the active site for iron binding, and the differences between the kinetics of the N- and the C-lobe. MD simulations on FbpA have led to the detailed observation of the binding kinetics of phosphate to the apo form, and to the conformational preferences of the holo form in conditions mimicking the environmental niches provided by the periplasmic space. To study the dynamics of these proteins with their receptors, one must resort to coarse-grained methodologies, since these systems are prohibitively large for atomistic simulations. Study of the complex of human transferrin (hTf) with its pathogenic receptor by such methods has revealed a potential mechanistic explanation for the defense mechanism that arises in the evolutionary warfare. Meanwhile, the motions in the transferrin receptor bound hTf have been shown to disfavor apo hTf dissociation, explaining why the two proteins remain in complex during the recycling process from the endosome to the cell surface. Open problems and possible technological applications related to metal ion binding-release in iron transport proteins that may be handled by hybrid use of quantum mechanical, MD and coarse-grained approaches are discussed.

## I2-What have we learned with computational tools in chemistry?

Viktorya Aviyente

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### *Effect of catalysts in pericyclic reactions*

The thermal and Lewis acid catalyzed cycloadditions of  $\beta,\gamma$ -unsaturated R-ketophosphonates and nitroalkenes with cyclopentadiene have been explored by using density functional theory (DFT) methods. Inspection of the thermal potential energy surface (PES) indicates that a majority of downhill paths after the bis-pericyclic transition state lead to the Diels-Alder cycloadducts, whereas a smaller number of downhill paths reach the hetero-Diels-Alder products with no intervening energy barrier. Lewis acid catalysts alter the shape of the surface by shifting the cycloaddition and the Claisen rearrangement transition states in opposite directions reversing the periselectivity of the cycloaddition giving a preference for hetero-Diels-Alder cycloadducts.<sup>1-2</sup>

### *Rationalization the role of catalysts in free radical polymerization reactions*

In this study, the effect of Lewis acid coordination ( $\text{ScCl}_3$ ) in controlling the stereoregularity during the free radical polymerization of N,N-dimethyl acrylamide (DMAM) has been investigated by Density Functional Theory (DFT). The strategy suggested in this study can be easily used by experimentalists in their endeavour of choosing the catalysts in order to end-up with the desired stereoregulation of the polymer chain.<sup>3</sup>

### *Degradation mechanisms in advanced oxidation processes.*

Advanced oxidation processes (AOPs) are based on the in situ production of hydroxyl radicals ( $\bullet\text{OH}$ ) and reactive oxygen species (ROS) in water upon irradiation of the sample by UV light, ultrasound, electromagnetic radiation, and/or the addition of ozone or a semiconductor. Diclofenac (DCF), one of the emerging organic contaminants (EOC), is of environmental concern due to its abundancy in water and is known to be subjected to AOPs. The current study uses density functional theory (DFT) to elucidate the mechanisms of the reactions between  $\bullet\text{OH}$  and DCF leading to degradation by-products.<sup>4</sup>

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## I3-GTP hydrolysis in the elongation factor EF-Tu

Bülent Balta<sup>1</sup>, Gülşah Çıfci<sup>2</sup>, Şeref Gül<sup>3</sup>, Mehtap Işık<sup>4</sup>, Selami Ercan<sup>5</sup>,  
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Elongation factor Tu (EF-Tu) is a G-protein responsible of the delivery of the aminoacyl-tRNA to the ribosome. EF-Tu has a low intrinsic GTPase activity. However, upon cognate codon-anticodon pairing, conformational rearrangements that catalyze the GTP hydrolysis take place. After GTP hydrolysis, EF-Tu leaves the aa-tRNA in the ribosome and moves away. In the literature, the reorientation of a conserved histidine (H85 in *T. aquaticus*) towards the active site is thought to be involved in the catalysis of GTP hydrolysis. Although in other G-proteins, an arginine is also involved, a corresponding residue was not identified on EF-Tu.

Molecular dynamics simulations, 200-300 ns long, have been carried out on the wild type and mutant EF-Tu·GTP complexes from *T. aquaticus* and *E. coli*. The Amber ff03 force field has been used, together with a periodic box of TIP3P water molecules.

In *T. aquaticus*, the Switch I region, an  $\alpha$ -helix near the active site, explores several conformations and R57 of Switch I enters the active site like the catalytic arginine in other G-proteins, suggesting a catalytic role for R57. On the other hand, pK<sub>a</sub> calculations via thermodynamic integration simulations show that an important fraction of H85 is doubly protonated and this residue spends a significant time in the active site even in the absence of ribosomes. This suggests that only the reorientation of H85 into the active site by the ribosome cannot account for the high stimulatory effect of the latter.

In order to determine the GTP hydrolysis mechanism and assess the contributions of H85 and R57, QM/MM calculations have been carried out. M06-2X and Amber have been used as the QM and MM methods, respectively.

## **I4-Molecular motion on metal surfaces: quantum and classical mechanical approaches**

Melihat Madran<sup>1</sup>, Alimet Sema Ozen<sup>2</sup>, Zehra Akdeniz<sup>2</sup>, Sondan Durukanoğlu<sup>1</sup>

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Today, molecular nanotechnology has reached such a level of sophistication that it seems possible to design and build artificial molecular machines like rotors, wheels, and motors. With the enhanced atomic scale techniques in imaging and controlling, there is a remarkable increase in experimental studies devoted to manipulation of molecules on the surfaces. However, controlled-manipulation of molecules and understanding the underlying molecular mechanisms in the process require atomic scale electronic structure calculations, potential energy surface scanning and molecular dynamics calculations. Such complementary calculations help not only fulfill the need in the area but also make significant contribution to the improvement of molecular nanotechnology. In this talk, I will discuss results of various atomic-scale computational calculations for investigating the observed translational and rotational motion of molecules on metal surfaces in great detail.

## **I5-Molecular dynamics simulations of biomolecules: Facing the challenges in connecting with biology**

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A primary role of computer simulations in biology is to complement high-resolution structural data from experiments with a dynamic perspective and ultimately connect to and explain biological function. Continuing challenges are how to reach biologically relevant time scales but also how to embrace the full biological complexity of cellular environments. Recent studies that highlight how both challenges can be addressed in modern simulations are presented. In the first example, the fundamental process of transcription in RNA polymerase II is analyzed via a combination of molecular dynamics simulations and kinetic network modeling to span a wide range of time scales. The results provide new insights into the mechanism by which RNA polymerase can achieve high RNA elongation rates while keeping errors due to nucleotide misincorporation to a minimum. The second example involves models at different levels of complexity of crowded cellular environments up to a comprehensive model of a bacterial cytoplasm. These systems were studied via molecular dynamics simulations to examine how constant non-specific interactions between macromolecules in such environments may affect the stability and dynamics of biological macromolecules. General findings are that the sampling of non-native conformations by proteins may be enhanced and that their diffusional motions are reduced drastically and highly depend on interactions with the local environment. Further insight is that solvent and metabolite properties are also significantly altered from dilute conditions. The simulation findings are discussed in the context of experimental measurements and methodological limitations.

# **I6-The linear response function of conceptual density functional theory: from mathematical properties to applications in single molecule electronics**

Paul Geerlings

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Within Density Functional Theory(1), the so called Conceptual Density Functional Theory (2) has proved to be a valuable tool for interpreting and predicting chemical reactivity. As opposed to the more traditional reactivity descriptors such as electronegativity, hardness,... the linear response function  $\chi(\underline{r}, \underline{r}')$  representing the response of the density  $\rho(\underline{r})$  at position  $\underline{r}$  to an external potential perturbation  $v(\underline{r}')$  at position  $\underline{r}'((\delta\rho(\underline{r})/\delta v(\underline{r}'))_N)$  remained nearly unexploited. Although well known, in its time dependent form, in the solid state physics and time-dependent DFT communities the study of the “chemistry” present in the kernel was, until recently, relatively unexplored.(3)

In this talk we report on recent investigations on both fundamental and applied aspects of the linear response function. Starting from its mathematical and physical properties (4)(5), its significance in discussing Kohn’s “Nearsightedness of Matter” Concept (6) we present recent applications on its role in the alchemical derivatives, at stake when exploring Chemical Space, in B,N substitution patterns of fullerenes, (7) and conclude by linking the linear response function to molecular electric conductivity at stake in single molecule electronics. (8)(9)(10)

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## **I7-A bridge between computational chemistry and environmental science**

Nilsun H. Ince

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The presentation aims to highlight the role of molecular and computational chemistry in advanced water treatment processes used in the destruction of recalcitrant contaminants in the water environment. Examples will be given based on hydroxyl radical-mediated advanced oxidation processes (AOPs), which are highly effective for the elimination of azo dyes and anti-inflammatory pharmaceuticals, both classified as “emerging pollutants” by the Environmental Protection Agency (EPA) of USA.

AOPs are based on the in-situ production of hydroxyl radicals ( $\bullet\text{OH}$ ) and reactive oxygen species (ROS) in water by irradiation of the sample with UV light, ultrasound, electromagnetic radiation, and/or by the addition of ozone or a semiconductor (Ref). Ultrasonic irradiation is a unique method in AOPs and based on the fragmentation of water molecules upon the implosive collapse of acoustic cavitation bubbles (ref). The result is generation of hydroxyl radicals and hydrogen peroxide, which promote the oxidative dissociation of organic molecules.

Decolorization of two reactive azo dyes C.I. Acid Orange 7 and C.I. Acid Orange 8 (the structures as given in Fig. 1) by ultrasound was modelled using DFT calculations and found that the attack of hydroxyl radicals onto the carbon that bears the azo linkage was preferred over that on the nitrogen atom. In addition, the difference in the rate of color decay of the two dyes despite similar structures was attributed to the competing reaction of hydrogen abstraction from the  $\text{CH}_3$  group [1].

Diclofenac (structure as given in Fig. 1) is a widely used anti-inflammatory pharmaceutical without prescription, but more than 80% of the compound is disposed of by urine, and bypasses the sewage treatment facilities due to its low biodegradability. It was found that sonication of diclofenac at near neutral pH by high-frequency ultrasound provided complete conversion of the compound, 45 % carbon, 30 % chlorine and 25 % nitrogen mineralization. DFT calculations confirmed that the major byproduct was 2,6-dichloroaniline, as identified experimentally and its formation was explained by  $\text{OH}\bullet$  addition to the ipso-position of the amino group. The stability of UV absorption at around 276–280 nm throughout the reactions agreed with the detected byproduct structures

(amino/amine groups; phenolic, aniline, benzene, and quinine-type derivatives). Microtox toxicity of the reactor aliquots at early reaction showed that initially the reaction products were very toxic; subsequently toxicity had a fluctuating pattern, and declined towards the “non-toxic” level after 90 min [2].

Modelling of the  $\bullet\text{OH}$ -mediated oxidation reactions by means of DFT calculations provided a good insight to the reaction mechanism. The results showed that the reactions were initiated either by the abstraction of a hydrogen or the addition of a  $\bullet\text{OH}$  radical to the parent molecule. However, the formation of organic radicals by  $\bullet\text{OH}$  attack was found to be kinetically and thermodynamically favored over the abstraction of hydrogen. [3].

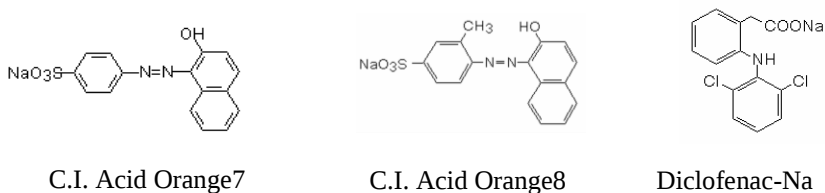


Fig. 1. Chemical structures of the test compounds

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## **I8-Molecular modeling of the reaction of deamidation in peptides and proteins using combined approaches**

G rard Monard

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The deamidation reaction is regarded as the most commonly observed chemical degradation which causes time dependent changes in conformation and limits the lifetime of peptides and proteins. The timed processes of protein turnover, aging, and several diseases (such as eye lens cataracts, Alzheimer, and particular types of cancer) have been suggested as possible consequences of deamidation. This reaction is also of significant chemical interest because of its effect on the stability of protein pharmaceuticals. Among the 20 natural amino acids, asparagine (Asn) and glutamine (Gln) residues are known to undergo spontaneous nonenzymatic deamidation to form aspartic acid (Asp) and glutamic acid (Glu) residues under physiological conditions.

Through a specific lens on the long standing collaboration between Viktorya Aviyente's group and the computational chemistry team of Nancy, we will review how molecular modeling can help in understanding the deamidation reaction of asparagine residues in small peptides and in proteins. Several theoretical and computational approaches will be presented, ranging from pure quantum mechanical studies to the modeling of free energy surfaces of reaction using combined QM/MM methods.

## **19-Predicting catalytic mechanisms of enzymatic reactions**

Maria João Ramos

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We know that we can establish catalytic mechanisms of enzymatic reactions and, in doing so, explain the findings of experimentalists, but can we actually predict them? This talk is concerned with the computational needs that we come across to figure out results within computational enzymology. Calculations devised to study protein interactions and circumvent problems in some relevant systems will be reported as well as recent developments in the establishment of some catalytic mechanisms. We have resorted to QM/MM (1,2) as well as other calculations (3,4), in order to analyse the energetics of processes related to the systems under study and evaluate their feasibility according to the available experimental data.

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## **I10-A comparative study of the polymer-nanotube interface through a reactive force field and density functional theory**

Hande Toffoli<sup>1</sup>, Ercan Gurses<sup>2</sup>, Hasan Gulasik<sup>2</sup>, Mine Konuk<sup>1</sup>, Elif Sert<sup>1</sup>, Gozdenur Toraman<sup>1</sup>

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As nanofabrication techniques progress, systems at the nanoscale find a rapidly increasing number of applications in various areas of technology. A particularly spectacular example of this phenomenon is carbon nanotubes (CNTs), tiny graphene sheets rolled up into single- or multi-walled cylinders. So far, CNTs have been used in diverse applications in device technology, drug delivery, field emission, air and water filtration, and many others. In addition to their unusual electronic properties, CNTs also possess extremely high axial strengths and are often used as strengthening agents in various host materials. In this talk, I will present results from a joint project run in the Aerospace Engineering and Physics Departments on the reinforcement of polymer matrices by carbon nanotubes. We conduct molecular dynamics (MD) and density functional theory (DFT) calculations to model the interaction between the polyetheretherketone (PEEK) polymer and single-walled CNTs. Our study serves not only to understand the physical properties of this novel interface such as adhesion energies, but also as a test of the REAXFF empirical potential (CHO and LG variants) against DFT studies. Following a brief introduction of the problem, I will first show results from our benchmark studies on the elastic properties of the two components separately, namely PEEK and CNTs. I will then present our finding on the interface, starting with a single polymer on a graphene sheet.

This work is supported by the Scientific and Technological Research Council of Turkey (TÜBİTAK) within the 1001 program, Grant No. 115M550.

# 111-1,3-Dipolar cycloaddition reactions of low-valent rhodium and iridium complexes with aryl nitrile N-oxides

Ilke Ugur<sup>1,2</sup>, Sesil Agopcan Cinar<sup>1</sup>, Burcu Dedeoglu<sup>3</sup>,  
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We performed density functional theory (DFT) calculations to model the reactions between low-valent Rh(I) and Ir(I) metal–carbonyl complexes and aryl nitrile oxides. These reactions possess the electronic and structural features of 1,3-dipolar cycloadditions. The Wiberg index which we calculated through NBO analysis indicates a partial double bond character of the metal–carbonyl bond thus the reaction is classified as a normal 1,3-dipolar cycloaddition involving M=C bonds. Analogous to their organic counterparts, the rates of formation of the metallacycloadducts are controlled by distortion energy. The cycloadduct products form a compact aromatic cyclic trimer between the PPh<sub>3</sub> ligands on the metal and aromatic ring on the 1,3-dipoles, which mainly participates to the stability of the complexes. Ir(I) complexes yield much more stable Ir(III) cycloadducts than their Rh analogues, due to the higher capacity of third-row transition metals to stabilize higher oxidation states. Overall, our calculations explain the ease of the chemical processes and the stabilities of the resulting metallaisoxazolin-5-ones.

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# POSTER PRESENTATIONS

*(Alphabetical order according to the last name of the  
presenting author)*

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# P1-Intermolecular interactions between mefenamic acid and saccharin

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Mefenamic acid (2-[2,3-Dimethylphenyl]amino]benzoic acid) (MEF) has been widely used as nonsteroidal anti-inflammatory drug for the pain treatment. Saccharin (benzoic sulfimide) (SAC) is known as an artificial sweetener. In current study, intermolecular photoinduced electron transfer in the MEF-SAC complex has been investigated to determine its structure and photophysical properties by using quantum chemical methods. The conformational analyses of investigated molecules were performed to determine initial structures. Full optimizations were performed with Gaussian 09<sup>1</sup> at the  $\omega$ B97XD/6-311++G(d,p) level. In order to explore the solvent effect, solvation calculations were performed by Tomasi's Polarizable Continuum Model (PCM)<sup>2,3</sup> using Dimethylformamide (DMF) as the solvent. Molecular orbitals and energy differences of frontier orbitals and electrostatic potentials (Figure 1) for studied molecules calculated at B3LYP/6-311++G(d,p) level in gas phase and in DMF. MEF-SAC complex is stable in the gas phase and DMF and shows intermolecular charge transfer between HOMO-LUMO orbitals by  $S_1$  excitation.

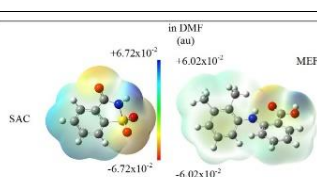


Figure 1. Electrostatic potentials of SAC and MEF in DMF

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## P2-Modeling of deacetylation reaction mechanism of o-acetylpeptidoglycan esterase with quantum cluster approach

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The O-acetylpeptidoglycan esterase (Ape1) from pathogen of bacteria *N-Gonorrhoeae* plays an important role in stages of the bacterial Oacetylation/deacetylation reactions. The O-acetylation of N-acetylmuramic acid (MurNAc) residues of peptidoglycan decreases the hydrolytic activity of lysozyme and lytic enzymes which are essential for bacterial life cycle. At this point, bacterial cell growth and controlled division entails deacetylation of the cell wall. O-acetylpeptidoglycan esterase (Ape1) enzyme which belongs to SGNH family catalyze the deacetylation of peptidoglycans and hence, was proposed to be a potential target for antibiotic development.<sup>1</sup>

The aim of this work was to perform a theoretical study on the deacetylation reaction mechanism of APE1 enzyme. For this purpose, the deacetylation reaction of APE1 enzyme with p-nitrophenyl acetate as a substrate was investigated with the quantum cluster approach using DFT. To provide further insight into the enzyme mechanism, a number of residues located in the proposed substrate binding sites of APE1 were included in the three different model clusters that varied in size (Figure 1), based on the X-ray crystal structure of the enzyme. In the smallest model (C0), SER80, ASP366 and HIS369 residues belonging to the catalytic triad of Ape1 were included. In the second model (C1), two important residues that were found in the oxanion hole and GLY324 and VAL325 residues surrounding the active site were also included to the system. The QM region was extended to 209 atoms for the last model (C2) and the reaction profile was found. In computational procedure, complete geometrical optimizations were performed at B3LYP/6-31G(d,p) level in the gas phase and D2 correction was added to include dispersion interactions. The final energies were refined by single point energies at a high level of theory with inclusion of solvent effects, as approximated by the polarized continuum model (PCM).

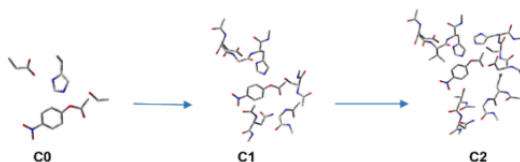


Figure. Schematic representation of the three different size DFT models of the active site of Ape1

<sup>1</sup>- J. M. Pfeffer and A. J. Clarke, ChemBioChem. **13**(2012)722-731.

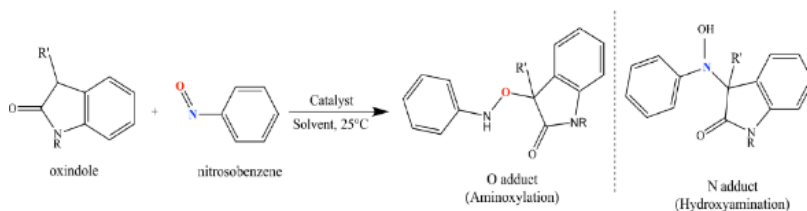
### P3-Determination of active organocatalyst using computational methods

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Number of reports on the use of small chiral organic molecules as catalysts and related computational efforts for understanding the origins of catalysis and selectivities keep growing. [1] Determination of highly efficient and selective organocatalytic structures rely on an expensive method involving the synthesis of a large number of derivatives followed by experimental testing of their activities. Quantum mechanical calculations have successfully uncovered numerous organocatalytic reaction mechanisms and explained the observed reaction outcomes; yet, study on highly complex multifunctional organocatalysts is still a challenging task due to the large number of conformational degrees of freedom. The purpose of this project is to allow easy and cost-effective determination of potential organocatalyst candidates for a target reaction using a new computational approach that combines the quantitative power of quantum mechanical calculations with drug design tools. The proposed method aims to allow the determination of organocatalysts with the desired three-dimensional arrangement of catalytic functional groups in an organocatalyst pool. Because the oxindole skeleton bearing a tetrasubstituted carbon at the 3-position is forming the core of many bioactive natural products and pharmaceutically active compounds [2], the development of chiral catalysts for their asymmetric synthesis is among the most actively studied topics in recent years. For this reason, for the application of the proposed approach in this project, the reactions of oxindoles with nitrosobenzene selected as targets. In the presence of amine catalysts, it gives two different products (hydroxyamination and aminoxylation products) and both of these products display different bioactivities and their selective synthesis is very important in pharmaceutical industry.



**Scheme 1.** Reaction of oxindole with nitrosobenzene

In this study [3], the factors affecting the reaction rate and product distributions in the reaction were investigated using quantum mechanical calculations. For this purpose, theoretical active site models were designed with alcohol/urea/thiourea functional groups and catalytic atom maps were generated using the arrangement of these pharmacophore groups in the active site models. The resulting catalytic atom maps were screened against a conformational library generated for cinchona alkaloid derivatives including dimers. Quantum mechanical calculations were used to determine the enantioselectivities of the matching organocatalysts and the catalysttransition structure interactions were analyzed. Based on the results of computations, catalysts were determined for synthesis.

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# P4-Resonances in the dielectronic recombination cross section of $\text{Ni}^{13+}$

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Radiative (RR) and dielectronic recombination (DR) rate coefficient are calculated for  $\text{Ni}^{13+}$  ion. The calculations are performed using atomic structure and collision code AUTOSTRUCTURE<sup>1</sup>. The problem is formulated within a multi-configuration Breit-Pauli(MCBP)<sup>2</sup> method within an independent processes, isolated resonance, and distorted wave approximation. The target configurations used to represent the ground state of the ion are:  $3s^23p^3$ ,  $3s^23p^23d^1$ ,  $3s^13p^4$ ,  $3s^13p^33d^1$ ,  $3s^23p3d^2$ ,  $3s^13p^23d^2$ ,  $3p^5$ , and  $3p^43d^1$ . Energy levels, radiative rates, and autoionization rates are calculated in both *LS* and *LSJ* couplings including the spin-independent mass-velocity and Darwin relativistic interactions. The  $(N + 1)$ -excited electron configurations are produced by coupling a Rydberg orbital,  $nl$ , or a continuum orbital,  $\epsilon l$ , to the  $N$ -electron target configurations with  $n$  values explicitly included up to  $n=25$  and a quantum defect approximation used for  $25 < n < 1000$ . Calculations are done for both intra ( $\Delta n = 0$ ) and inter shell ( $\Delta n = 1$ ) core excitations. Total DR and RR rate coefficients corresponding to  $\Delta n = 0$  and  $\Delta n = 1$  inter and intra shell core excitations calculated within LSJ coupling scheme are plotted in Figure 1(a) with labels MCBP\_DR (RR). DR rates are compared with the recommended data from Mazzotta et al.<sup>3</sup>

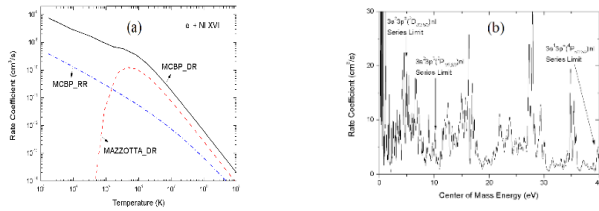


Figure 1: (a) Total DR and RR rate coefficients for  $\text{Ni}^{13+}$  is compared with Mazzotta's recommended results. (b) Resonances arising from  $\Delta n = 0$  inter shell core excitations.

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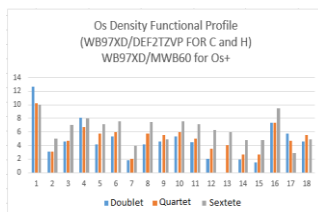
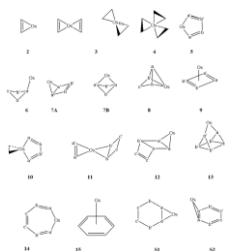
# P5-Os cation assisted transformation of acetylene to diatomic hydrogen

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Schwarz and co-workers<sup>1</sup> have shown that certain metal cations catalyze conversion of acetylene to benzene in the gas phase. Altun et al.<sup>2</sup> modeled the process for iron cation, and established the structures of  $\text{Fe}(\text{HCCH})_n$  cation with  $n=1, 2$ , and  $3$ . Cyclized forms of  $\text{Fe}(\text{C}_4\text{H}_4)$  cation can form with only small kinetic barriers; the Fe-benzene complex cation is the lowest energy structure. In the gas phase this species has enough vibrational energy to dissociate and produce free benzene. Heavier metal cations, osmium in particular, follow a different reaction path with acetylene. Production of diatom hydrogen is observed. In such cases the CH bonds in a metallocyclic  $\text{C}_6\text{H}_6\text{Os}$  cation are activated, showing substantially lowered CH stretching frequencies. We trace the reaction path for extrusion of hydrogen in two different density functional models. In both model we used wb97xd functional. In the first model def2tzvp is used as the basis set for all atoms. In the second model osmium cation is represented by the relativistic pseudopotential MWB60. The reaction efficiency seems to be high for the Os system. The species considered in this work and their energy profiles with respect to the doublet spin symmetry of the species 15 are shown in the chart below. Species 1:  $\text{Os}(+) + 3\text{Acetylene}$ .



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# P6-Double fluorescence assay via a $\beta$ -cyclodextrin containing conjugated polymer as a biomimetic material for cocaine sensing

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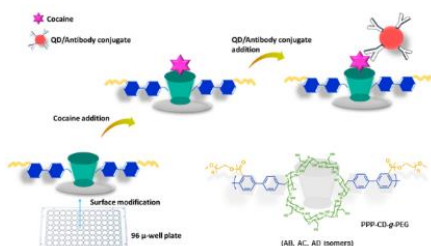
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A double fluorescence  $\mu$ -well assay that exploits a novel conjugated polymer containing cyclodextrin (CD) as the key component is reported. For the construction of the cocaine bioassay, poly(*p*-phenylene) with CD units in the main-chain and poly(ethylene glycol) side chains (PPP-CD-*g*-PEG) was first prepared by Suzuki coupling polymerization and coated on each well as a biomimetic material<sup>1</sup>. Although the polyphenylene backbone is responsible for the fluorescence properties without an additional fluorophore, PEG and CD provide water solubility and selective complexation with cocaine, respectively. A cocaine antibody was used as a secondary recognition compound after labelling with quantum dots (QDs). Most notably, we show that the two-color fluorescence nature of the assay facilitates double measurement from the same sample and the described strategy can be adapted to various sensing systems.



**Scheme 1.** Schematic representation of the construction of  $\mu$ -well assay by using PPP-CD-*g*-PEG as covering material.

## References



## **P8-Mechanistic DFT study on one-pot synthesis of heterocyclic compounds**

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Heterocyclic compounds having pharmacological, pesticides, antimicrobial features constitute biologically active groups. It is known that the reason for very important biological activities of this type of heterocyclic organic compounds is because of the presence of their characteristic N-C-O groups. On the other hand, C-C and C-heteroatom bond-forming reactions are very important for organic synthesis. The aim of our study is to perform one-pot synthesis of biologically active new heterocyclic compounds derived from aldehyde, amine, acetylketene via cycloaddition reactions and to investigate the proposed mechanisms using DFT.

All stationary points belonging to each step were optimized and av in the gas phase with the density functional M06-2X method using 6-31G(d,p) basis set implemented in Gaussian 09. To take into account the solvent effect, single-point energy calculations with the polarizable continuum model (PCM) were carried out at the M06-2X/6-311++G(d,p) level with dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>) as solvent, since this solvent was used in the experimental study. All possible cyclization pathways have been considered in order to shed light on the mechanism.

We acknowledge the Scientific and Technological Research Council of Turkey (TUBITAK, project no. 112T880).

## P9-Selectivity in (4+3) cycloadditions of furfuryl cations

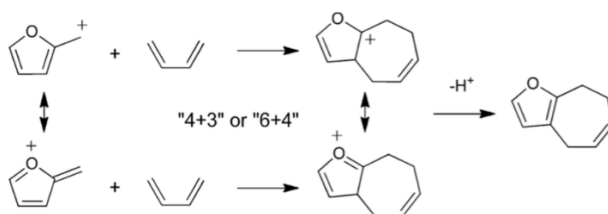
D. Hertsen<sup>1</sup>, Ö. N. Avci<sup>2</sup>, B. Denoo<sup>3</sup>, V. Van Speybroeck<sup>1</sup>, J. M. Winne<sup>3</sup>, S. Catak<sup>1,2</sup>

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Scheme 1. (4+3) Cycloadditions of Furfuryl Cations

Furfuryl cations are reliable three-carbon dienophiles for a wide range of conjugated dienes and can be generated from simple furan-2-methanol derivatives (furfuryl alcohols) as versatile organic building blocks for the elaboration of complex fused-ring systems.<sup>1,2</sup> The mechanism of this orbital symmetry-allowed oxyallyl-type (4+3) cycloaddition<sup>3,4</sup> was investigated in this work, where we have examined highly selective intermolecular furfuryl cation cycloadditions from a joint experimental and theoretical perspective. Density Functional Theory (DFT) calculations have been performed with the Gaussian 09 software package using the M06-2X/6-31+G(d,p) utilizing a continuum solvent environment. The factors leading to the experimentally observed selectivity were thoroughly explained.

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## P10-Unexpectedly synthesis of copper salen complexes from salicylaldehyde thiosemicarbazone

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Tülay Bal-Demirci<sup>1</sup>

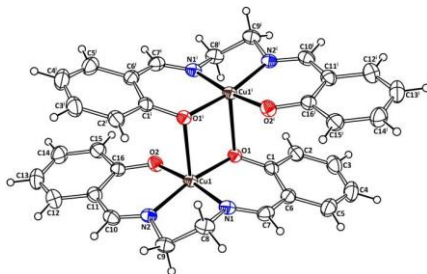
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Schiff bases and salens have been popular ligands of metal complexes with potential biological activity, such as anti-inflammatory, antifungal, antimicrobial, antiviral and antioxidant [1]. N,N-bis(salicylidene)-R-diamine (R:aromatic, aliphatic) and its derivatives are known as salens. The Salen complexes are important in coordination chemistry because of the photophysical properties and the activities of biological and catalytic [2].

In this study, the unexpectedly synthesis of salen complex was carried out by the reaction of the salicylaldehyde thiosemicarbazone with ethylenediamine in the presence of Cu(II) ion. The structure of the complex was characterized by elemental analysis, IR and single crystal X-ray diffraction.



# **P11-Identification of novel MDM2-p53 protein-protein interaction inhibitors with multidimensional molecular modeling approaches and application of binary QSAR models for prediction of therapeutic activity and toxic effects**

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**Background:** The tumour suppressor protein P53 plays an important role in regulation of cell cycle, DNA repair and apoptosis.<sup>1–4</sup> The majority of human cancers are caused by mutations or deletions of alleles in p53.<sup>1–6</sup> P53 activity is effectively inhibited by its negative inhibitor Murine Double Minute 2 (MDM2) oncogenic protein (Figure 1 and 2). The presence of excessive MDM2 in cells has been determined to cause in ~11% of all tumours and observed at higher levels in certain tumour types such as hepatocellular carcinoma (44%), soft tissue sarcomas (31%) and osteosarcomas (20%)<sup>3,7</sup>. Therefore development of suitable MDM2 inhibitors is crucial for better anticancer treatments in future.

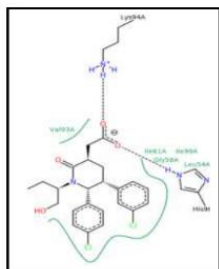
**Method:** MDM2 protein (PDB:4HBM) was chosen and prepared by using protein preparation module of Schrodinger's Maestro Molecular Modeling Suit.8 Hydrogen atoms were added, missing side chains and loops were fixed using Prime module of Maestro. Protonation states of amino acid residues were determined by PROPKA at physiological conditions.<sup>9–10</sup> Water molecules around the catalytic side were kept during protein preparation and rest of the water molecules were removed. Optimization were performed by QPLS\_2005 force field. 176.000 drug-like ligands were retrieved from the Otava Drug-Like Green Collection Chemical Database (OD). The protonation states of screened small-molecules were determined using LigPrep module of the Maestro8 at physiological conditions. Docking simulations with Glide/SP method were performed for 176000 molecules. Subsequently, the top-100 ligands has to their high docking scores with Glide/SP method and further docking studies Glide/XP, IFD, QPLD and GOLD methods were performed to elucidate the relative performances of the methods in exploring interactions of selected ligands with the target when compared to known MDM2 inhibitors. For the same set of ligands, topology-based binary QSAR models (prediction of therapeutic activity and toxic effects) analyses were also applied with MetaCore and MetaDrug tools to predict their first and second-pass metabolism, therapeutic activities, toxicity properties.

**Results:** Among the studied ligands, some of them showed better binding behavior than standard inhibitors against MDM2 protein. Their topology-based analyses showed that these ligands could exhibit better therapeutic activity and / or less side effects than some of known MDM2 inhibitors.

**Conclusion:** Some of the studied ligands bind more tightly than the standard inhibitors to MDM2 protein. They display strong interactions with the amino acids known to be critical. Although it is too early to consider them as MDM2 inhibitors and anticancer drug candidates, the results obtained so far are very promising.



**Figure 1** Crystal structure of MDM2 (PDB:4HBM)



**Figure 2** Interactions in MDM2 Crystal Structure (PDB:4HBM)

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## P12-Reactivity descriptors for the prediction of the degradation reactions of sulfonamides

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Antibiotics have been largely used in human and veterinary medicine, as well as in the feeding of domestic animals [1]. As an important antibiotic class, sulfonamides are extensively used in the pharmaceutical industry and in the chemical industry as dyes and artificial fibers [2]. However, due to their high resistance to the photodegradation and biodegradation, these kinds of pharmaceuticals were often excreted into sewage with metabolites as well as the unchanged parent compounds after usage. These discharged sulfa pharmaceuticals have been frequently detected in a variety of aqueous media, such as effluents of wastewater treatment plants, surface water and even drinking water [2,3]. Therefore, there is a need for certain molecular descriptors to predict the reactivity of sulfonamides.

In this study, the structures of 22 sulfonamides were investigated theoretically with the intention of finding certain molecular descriptors to predict the degradation potency for aqueous media. Conformational analyses and geometry optimizations of all the structures were performed to determine the most stable structures. Modeling of the molecules was performed with DFT at B3LYP/6-311++G\*\* level. The solvation effects were computed using CPCM. The electronic energies, electron densities, molecular charge distributions of the molecules and the DFT reactivity descriptors such as chemical hardness, softness, electronegativity, fukui functions for all the molecules were calculated.

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# P13-Cytotoxic activity and synthesis of nickel (II) mixed ligand complex of 4-methoxysalicylaldehyde thiosemicarbazone with *N,N*-diethylethylenediamine

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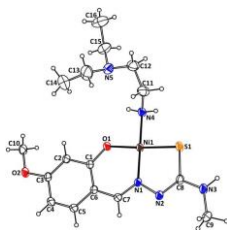
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Thiosemicarbazones are an important class of Schiff bases. The thiosemicarbazones and their metal complexes have been subject of analytic and catalytic studies because of structural properties and of medicinal studies because of their biological potentials [1-3]. In this study, it was synthesized and characterized mixed-ligand nickel(II) complex of 4-methoxysalicylaldehyde thiosemicarbazone with *N,N*-diethylethylenediamine in the presence of nickel (II) ion. The properties and structures of ligand and complex were investigated by elemental analysis, IR, <sup>1</sup>H-NMR and single crystal X-ray diffraction. Cytotoxic effects of the compound was evaluated by MTT test for K562 chronic myeloid leukemia cell line and the compound has shown significantly cytotoxic effect by reducing cell viability.



The mixed-ligand nickel(II) complex of thiosemicarbazone

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## P14-A novel methodology to predict plasticization pressures of polymeric membranes

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Plasticization is a pressure dependent phenomenon and occurs when the concentration of these gases in the polymer reaches a critical value to swell the material, disrupt chain packing and increase fractional free volume (FFV) and inter-segmental mobility [1]. Since experimental determination of the plasticization pressure requires high-pressure experiments, screening all polyimide and copolyimide structures experimentally is an expensive and time consuming work [2]. In this study novel methodology is developed to predict CO<sub>2</sub>-induced plasticization behaviour of glassy polymers using fully atomistic simulations. It is based on quantum-level charge calculations and sorption-relaxation cycles comprising integrated molecular dynamics (MD) and Monte-Carlo (MC) simulations. CO<sub>2</sub> accessible free volume with the presence of CO<sub>2</sub> (CAVF+), is the phenomenon introduced and used in plasticization pressure predictions. The methodology that is proposed in this study allows computationally cheaper and accurate estimations of plasticization pressure of polymers to be used in gas separation processes.

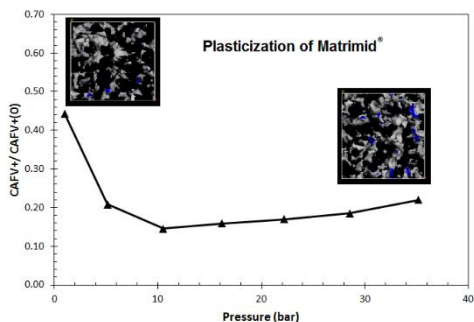


Figure 1. Plasticization behaviour of Matrimid

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## **P15-Rationalization of the activity of the lactone form of topotecan towards the DNA/topoI complex**

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Human Topoisomerase I (TopoI) is a type-I enzyme that relaxes the supercoils on the DNA structure. First, it creates a nick only on one strand of DNA by covalently binding to it, and the relaxation process then performed by rotating the nicked strand around the intact one and re-ligating it back. Camptothecin (CPT) and its derivatives are small drug molecules that are known to target only Topoisomerase enzymes, which explains the reason why they are getting attention from the research groups. When CPT or its analog Topotecan (TPT) is added to DNA-TopoI complex, the drug intercalates where the nick occurs and prevents supercoil relaxation by turning TopoI into a DNA-damaging agent.<sup>1</sup> TPT is a small molecule with 6 fused-ring structure and has two forms: lactone and carboxylate forms, which are in equilibrium at neutral pH. It was shown that the lactone form is the “active” form of the drug, however, in the crystal structure of ternary complex (TPT-DNA-TopoI) obtained by Staker et al (2002)<sup>2</sup> both forms were intercalating between the bases of DNA at the same site. This finding raises the question regarding the cause of the activity difference between two forms despite binding to the same site. In this study, using Molecular Dynamics (MD) and hybrid Quantum Mechanics/Molecular Mechanics (QM/MM) approaches the cause of the difference in activity is investigated. 450ns long MD simulation of both forms was performed and interaction energies of these drugs were calculated using QM/MM method by choosing TPT as QM site. Decomposition of the interaction energies showed that the interaction with TopoI is the reason for their activity difference. When the contribution of residues on the interaction energy was investigated, it was found that the most striking effect was due to K532 residue, and the topological analysis has further supported this finding. In addition, when the hydrogen bond networks around the drug were investigated, it was observed that in lactone form K532 was interacting with the drug, which was lost in carboxylate form. In conclusion,

lactone form of TPT is held by K532 residue strongly and N722, T718 and DTT10 base create a hydrogen bond network around the binding pocket in the lactone form that further stabilizes the lactone TPT.

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## P16-Computational design of small organic molecules as mimics of hydrolase enzymes

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Development of new green catalysts displaying the catalytic power of enzymes is one of the most widely explored topics in recent years. Recently, in collaboration with the Schafmeister group at Temple University, new transesterification catalysts called spirooligozymes were developed, by placing the catalytic machinery of esterase enzymes onto modular spiro-fused bispeptides with the help of quantum mechanical transition state calculations using the “inside-out” approach.

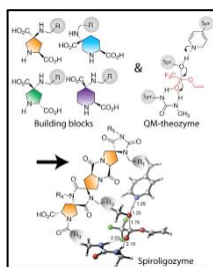


Figure 1. “Inside-out” approach to catalytic spirooligomers<sup>[1]</sup>

The key to the catalytic power of esterase enzymes is the proton shuttle mechanism acting between Ser-His-Glu nucleophilic triad in their active sites. The increased basicity of histidine in the presence of glutamate allows the abstraction of proton from serine activating it as a nucleophile. The high activities of these enzymes are linked to the high level structural and electrostatic pre-organization of this catalytic machinery in their active sites. In the designed spirooligozymes, the catalytic active site of esterase enzymes was represented by pyridine-alcohol dyad. The best-developed spirooligozyme increased the rate of transesterification reaction between vinyl trifluoroacetate and methanol by 2200-fold for the first step and by 130-fold for the second step. However, quantum mechanical calculations demonstrated that, the catalytic groups in spirooligozymes sample numerous alternative conformations beside the active one and the H-bond network required for efficient catalysis is not maintained<sup>[2]</sup>. These computational results suggest that the activities of spirooligozymes can be

significantly improved by providing a high-level pre-organization of the catalytic function groups. The purpose of this study is to identify the structural modifications that could allow the elimination of non-reactive conformations of spiroligozymes and to determine spiroligozyme derivatives with high level structural pre-organization for efficient catalysis. To achieve this aim, Medchem transformation tool was applied for the generation of a derivative library and a conformational search was performed for selected derivatives, which were further evaluated by quantum mechanical calculations.

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## **P17-Construction of allosteric residue networks in caspase-7 using energy perturbation responses**

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The discovery of caspases and their involvement in cancer and neurodegenerative disorders lead pharmaceutical studies to focus on these molecules as drug targets. A thiol-containing small molecule binding to the allosteric site at the dimer interface induces a shift in loop positions and traps the molecule in a conformation that resembles the pro-caspase form. In order to understand the communication among the allosteric residues and the active site residues of these molecules, we performed energy perturbations on allosteric residues of caspase-7 based on the energy dissipation model<sup>1,2</sup>. We compared four mutated (G188P, G188L, 187W and R187M)<sup>3</sup> and wildtype structures aiming to detect the effect of single mutations on energy dispersion. First, traditional molecular dynamics (MD) simulations were performed, using NAMD<sup>4</sup> software and CHARMM27<sup>5</sup> force field for 100 ns. Energy perturbations were applied in the form of velocity increase of a chosen residue. The energy difference between a perturbed and an unperturbed simulation was calculated for each residue and then the time of the energy change of a residue is recorded as that residue's response time. Allosteric residue networks were constructed based on these obtained response times.

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# P18-Dye and semiconductor interfaces under scrutiny: cluster versus periodic approach for electron injection and light harvesting

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Exploitation of solar energy for sustainable development is of great interest in recent years as illustrated by the significant number of investigations on solar cells.<sup>1</sup> To provide a low-cost alternative to silicon and other inorganic-based photovoltaic devices, employing fully organic dyes as sensitizers has recently gained considerable attention, following Gratzel's invention of Dye-Sensitized Solar Cells (DSSCs).<sup>2</sup> In this study, we report a theoretical investigation, probing the effective modeling of dye@TiO<sub>2</sub> interfaces while benchmarking distinct computational methods. The selected organic dyes were previously synthesized<sup>3</sup> and their optical properties as standalone dyes were computationally investigated.<sup>4</sup> Density functional theory (DFT) calculations have been performed to elucidate the dye → semiconductor electronic injection process –the first step of charge generation in solar cells. Projected density of states (PDOS) have been obtained by means of two main approaches: 1) single dye@SC model, 2) dye@SC model with periodic boundary conditions, and have been analyzed in a comparative manner. In addition to periodicity, effects of solvation, inclusion of non-covalent interactions, and different DFT functionals have been scrutinized within the framework of organic dyes.

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## P19-A computational approach to sustainable industrial amines

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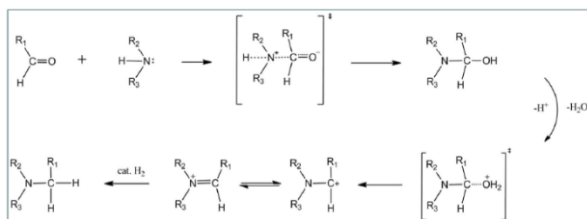
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Green chemistry approaches and utilization of natural products from sustainable sources are becoming more and more relevant in the industrial applications. Investigation of a facile and more efficient route for a hydroaminomethylation process is of great interest to the chemical and pharmaceutical industry. This process involves a sequence of processes going from hydroformylation, amination of the obtained aldehyde and finally hydrogenation of the enamine to produce saturated long chain amines.

In this work, the reductive amination of aldehydes to secondary amines was investigated by use of computational approaches. Generally, reductive amination reaction is a nucleophilic addition between the carbonyl compound of aldehydes and ketones, and a variety of primary and secondary amines. The initial step of the reaction includes the formation of a hemiaminal. In a subsequent condensation reaction this intermediate forms an imine or an iminium ion depending on the pH of the reaction medium. The equilibrium between aldehyde/keton and imine can be influenced by removal of the released water. At the final step, the desired amine is produced by reduction of the imine. The formation of the imine plus subsequent reduction by a hydride can be performed in a single reaction vessel.

There are several proposed mechanisms in the literature about indirect or direct reductive amination, depending on pH and thus the protonation state of the imine (Scheme 1). Hereby, the reaction between long chain dodecanal (C<sub>12</sub>H<sub>24</sub>O) and diethylamine was investigated in different protonation states. The energy profile for the uncatalyzed, explicit water assisted and acid catalyzed reactions and all transition states were characterized by MP2 calculations. Single point solvent calculations were carried out on each system in order to estimate the effect of solvent on the reaction profile.



Scheme 1. Proposed mechanism for the reductive amination of aldehydes.

## **P20-Effect of temperature on the molecular dynamics simulations of HLA-A\*02 alleles**

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Understanding the mechanism of the peptide immunogenicity is important for the design of peptide-based vaccines [1][2]. Therefore, investigation of the characteristic dynamics of Human Leukocyte Antigens (HLAs) may offer significant insights into the mechanism of initial steps in T-cell activation which is a key event in immune response [3]. The peptide immunogenicity is also known to be related to the stability of peptide-HLA complex [4].

In this study, in order to investigate the stability of immunogenic peptide-HLA complexes and the residues playing key roles in binding stability, various computational techniques have been employed. Initially, computational dockings were applied to model the two immunogenic peptides-HLA-A\*02:01 complexes [5]. 100 ns parallel molecular dynamic simulations were then conducted on these models at two different temperatures via GROMACS 5.0.1 software [6].

In our calculations, HVDGKILFV peptide is found to be stable at 310 K whereas it is unstable at 473 K. On the other hand, SLSAYIIRV peptide is found to be stable at both temperatures. Our computational results are found to be in good agreement with the previous findings [5]. While, HVDGKILFV peptide has one anchor residue at P9 position, SLSAYIIRV peptide has two anchor residues at P2 and P9 positions. These variations between the peptides can be related to their observed stability [5] differences on the cell surface.

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# P21-Ab initio study of novel phthalocyanine – based covalent organic frameworks

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We report the theoretically predicted structures having the 2D-network topologies for novel phthalocyanine – based covalent organic frameworks (COFs). COFs are new emerging functional porous materials held together by strong covalent bonds which result in molecular building blocks that can be arranged in layered 2D or 3D periodic networks. 2D frameworks are built up from nodes (organic or metal-organic compounds) and linkers which are organic molecules. The out-of-plane  $\pi$ -interactions in 2D COFs induce a large electronic coupling between the  $\pi$ -orbitals of the stacking layers. This electronic coupling facilitates the transport of charge carriers and excitons, giving rise to the semiconducting, optoelectronic, and photoconductive nature of COFs [1]. It is known that COFs may adopt either eclipsed arrangement of a layered structures of planar sheets or staggered ones. For eclipsed structure the stacking offers macrocycle-on-macrocycle and linker-on-linker arrangement and this is the typical packing for the COFs while for staggered structures the planar sheets of adjacent layers are offset by half of unit cell distance along the one of the axis. A self-consistent ground-state calculation were performed with the ABINIT code [2] to simulate these two extreme packing possibilities. The obtained models were evaluated using the Accelrys'Reflex Plus software package for crystal structure determination from powder X-ray diffraction, implemented in environment of Materials Studio (MS) Modelling [3]. It was found that practically all studied COFs belong to staggered structures.

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# P22-Rh-catalyzed [5+1] and [4+1] cycloadditions of 1,4-enynes by CO with concomitant 1,2- versus 1,3-acyloxy migrations: a DFT study

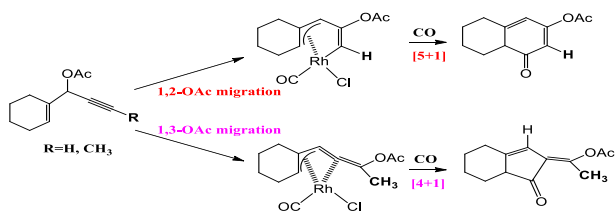
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The mechanisms of the  $[\text{RhCl}(\text{CO})_2]_2$ -catalyzed intramolecular cycloadditions of 3-acyloxy-1,4-enynes (ACEs) by CO with concomitant acyloxy (OAc) migrations have been extensively investigated using density functional theory (DFT) calculations at the B3LYP/6-31+G(d) level (LANL2DZ for Rh). Intra- and intermolecular cycloadditions of 3-acyloxy-1,4-enynes (ACEs) enable the formation of various substituted cyclic compounds via acyloxy migration. The ACEs with terminal alkynes or electronically demanding alkynes favor a Rautenstrauch 1,2-acyloxy migration and subsequently undergo [5+1] cycloaddition by carbonylation whereas ACEs with other internal alkynes prefer a Saucy-Marbet 1,3-acyloxy migration, followed by [4+1] cycloaddition with CO by the catalysis of various metals.<sup>1,2</sup> Recently, rhodium metal has been successfully used in the literature. As it is seen in **Figure 1**, Rh(I)-catalyzed cycloadditions of ACEs lead to functionalized cyclohexadienones and cyclopentenones with terminal and internal alkynes, respectively.<sup>2</sup> In this study, the experimentally observed product distribution could be explained and the acyloxy migration was found as the rate determining step from the DFT calculations.



**Figure 1.** Rh-Catalyzed Competitive 1,2- versus 1,3-Acyloxy Migration Followed by [5+1] and [4+1] Cycloadditions of 1,4-enynes with CO

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## **P23-Theoretical investigation of the degradation mechanism and byproduct assessment of diclofenac**

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Diclofenac (DCF) is an anti-inflammatory non-steroidal medication used widely for the remediation of rheumatic and arthritic pains. Because of its persistent occurrence in fresh water environments owing to poor degradation in sewage treatment and its potential toxicity towards several aquatic organisms (e.g. fish and mussels), diclofenac is an emerging contaminant. The present work aims to propose the initial reactions of diclofenac with •OH to elucidate the mechanism of subsequent reactions that yield the most common degradation byproducts reported in the literature. Density functional theory (B3LYP/6-31+G(d)) is used to rationalize the reaction mechanisms for the formation of the byproducts detected experimentally. The study also encompasses estimation of acute toxicities of the intermediates to assess the potential risk of the parent compound and its oxidation byproducts in the aquatic environment.



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## P25-Assessing the Ligand-protein Binding Modes with Computational Tools

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Designing small molecules with desirable binding affinity and biological activity is one of the major goals in computational biology.<sup>1-4</sup> An important goal of computational medicinal chemistry is to develop methods that accurately can estimate the free energy of binding,  $\Delta G_{\text{bind}}$ , which allows to predict the binding strength of any drug candidate without synthesizing it. Computational methods that combine molecular mechanics energy and implicit solvation models, such as Molecular Mechanics/Poisson-Boltzmann Surface Area (MM/PBSA) and Molecular Mechanics/Generalized Born Surface Area (MM/GBSA), have been widely used in free energy calculations.<sup>1-3</sup> Compared with rigorous methods such as Free Energy Perturbation and Thermodynamic Integration,<sup>4</sup> MM/PBSA and MM/GBSA are computationally more efficient.<sup>5</sup>

In this study, the inhibition of phosphodiesterase (PDE) enzymes, which are responsible for the breakdown of adenosine 3',5'-monophosphate (cAMP) will be investigated.<sup>6</sup> The potentially clinical benefits of PDEIV inhibition require to design novel inhibitors for PDEIV enzyme with less side effects than known potent PDEIV inhibitors. For PDEIV-ligand complex, the PDEIV selective inhibitor rolipram, whose X-ray structure is co-crystallized with PDEIV (pdb code: 1RO6) will be used. The experimental binding free energies of rolipram ( $\Delta G_{\text{exp}} = -49.66$  kJ/mol) and a few other ligands that are known from the experimental IC<sub>50</sub> results of Dal Piaz et al.<sup>7</sup> will be tested for PDBIV (1RO6) and its complex. Then, the same procedure will be repeated for the complexes with ligands proposed in our earlier work<sup>8</sup> and the knowledge of calculating binding Gibbs Free energies will be extended to further studies.

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## P26-Modeling of homogeneous catalysis reaction of C-H bond activation

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A catalyst is a substance that increases the rate of a chemical reaction by reducing the activation energy, but which is left unchanged by the reaction. Thus, catalysis plays a critical role in accomplishment of industrially significant chemical transformations, by requiring less energy investment in underlying processes [1]. For inorganic chemists, homogeneous catalysis is often synonymous with organometallic catalysts. CH activation may be defined as a reaction that cleaves a carbon-hydrogen bond. It can be considered to be the binding of a substrate to a metal center. Catalysts that are able to activate CH<sub>4</sub> at lower temperatures are therefore most important for the direct synthesis of CH<sub>3</sub>OH. In 1970s, Shilov showed that methane could be converted to methanol with Pt(II) and Pt(IV) complexes. The addition of Pt(IV) to the aqueous reaction of PtCl<sub>4</sub><sup>2-</sup> with methane lead to the production of selectively oxidized species methanol and methyl chloride [2]. Periana et al. made Shilov-like chemistry which is much more efficient in a series of methane conversion catalysts [3]. Organometallic approaches to methane conversion became a subject mainly after the work at Periana et al. The activation of methane with gas phase OsO<sup>+</sup> for dehydrogenation and dehydration mechanisms has been investigated in this study. Potential energy surfaces for the dehydrogenation reaction and dehydration reactions were investigated. In addition a preliminary computational study of stability and thermodynamics of the OsO<sup>+</sup> type catalyst for activation methane to methanol was conducted. The results showed that the first activation of hydrogen bond is not thermodynamically favored. Thus, this observed behavior can be our guide to seek various reaction mechanism which are feasible.

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# P27-A DFT study on electronic and optical properties of BTI-based oligomers

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Recently, a series of high-mobility polymeric semiconductors as new materials, suitable for organic field effective transistor (OFET) devices were synthesized.<sup>1,2</sup> However the questions related to their processability and environmental stability, as well as their applicability for OFET devices remained unclear. In this study, the properties of synthesized bithiophene-imide (BTI) (Figure 1) based organic molecules were studied by using the Density Functional Theory (DFT) and Time-Dependent DFT (TD-DFT) methods at B3LYP/6-311+g(d,p) level of the theory. Firstly, the molecules (comonomers) synthesized by combining the BTI unit with different aromatic benzene or thiophene rings were modeled. Then, the electronic and optical properties of comonomers, their dimers and the effect of the  $R_1$  groups (Figure 1) and the chain length of the backbone on the aforementioned properties were investigated.

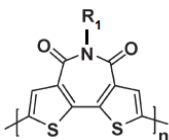


Figure 1. Bitiyoferenimid (BTI) monomer unit ( $R_1$ : H,  $\text{NO}_2$ ,  $\text{NH}_2$ , OH, F, Cl, Br, I)

The effects of  $R_1$  substitution and lengthening of the chains due to the dimerization on the UV-VIS spectra of the studied molecules were analyzed and the spectral shifts were discussed. This study will form a basis for the forthcoming molecular dynamics (MD) simulations which will be carried out to elucidate the thin film properties of these materials.

This work was supported by TUBITAK (project № 115Z501).

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## P28-Dioxygen activation by $[\text{Ni}(\text{H})(\text{OH})]^+$ , an MCSCF study

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Multi reference quantum chemical calculations utilizing MCQDPT2 and CASSCF methods, are used to examine the activation mechanism of dioxygen with  $[\text{Ni}(\text{H})(\text{OH})]^+$  complex. The activation of dioxygen molecule by  $[\text{Ni}(\text{H})(\text{OH})]^+$  complex is reported in previous experimental work[1] and following theoretical studies[2] expressed that the quartet state of the complex is reactive while the doublet state is inert. The quartet state owed its reactivity to non-innocence of the hydroxyl ligand. Here, the process up to hydroperoxide byproduct which has a key role on formation of the products is described. Initial encounter complex having sextet, quartet and doublet spin symmetry is analyzed at complexation step of the reactants. Electron transfer from the Nickel center to the redox active OH ligand was investigated. Effective spin surface of the reaction is specified as quartet, doublet state is not reactive. Crossing point calculations are done between potential energy surfaces of different spin surfaces which are energetically close. A crossing point is identified between initial encounter complexes on sextet and quartet spin surfaces. Spin-orbit coupling calculations are carried out in order to get an idea about surface hopping.

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## P29-Computational assessment of iron release from the N- and C-lobes of human serum transferrin

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Human serum transferrin (hTf) binds ferric ions with high affinity and delivers them into cells via receptor-mediated endocytosis upon a decrease in pH in the endosome.<sup>1</sup> Protonation events and conformational changes are known to play an important role in iron-release mechanism though the release mechanism is not yet fully understood.<sup>2</sup> hTf consists of two similar lobes which release iron at different rates. In this study, we investigate the iron binding sites of N- and C-lobes using quantum mechanical tools. The protonation of axial tyrosine is proposed as the potential route for the release of iron in both lobes and proton transfer pathways are suggested for the protonation of this tyrosine (Figure 1). The energy difference between the complexes displaying the protonation of the axial tyrosine (Tyr188 and 517 respectively in N- and C-lobe of Tf) around  $\text{Fe}^{3+}$  suggests that the release of iron in the N-lobe is thermodynamically driven, in contrast to the C-lobe, supporting the experimentally observed higher release rate of iron in the N-lobe in the absence of the Tf receptor.

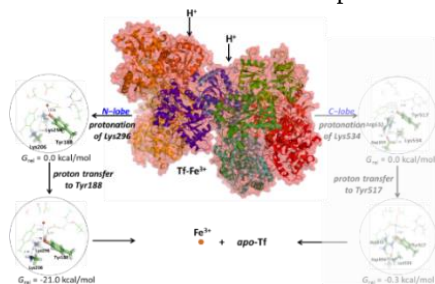


Figure 1. Proposed iron release mechanisms in the iron binding site of N- and C-lobes of human serum transferrin.

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## P30-Structure-reactivity relationships in sulfur-centred radical chemistry: a computational study

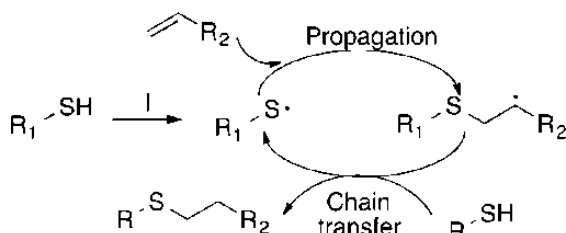
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In recent decades, there has been growing interest in sulfur-centred radical containing reaction mechanisms, such as thiol-ene polymerization reactions. This particular technique yields uniform polymer network structures with high and narrow T<sub>g</sub> values and low polymerization shrinkage stress, among other advantages<sup>1</sup>. Thiol-ene reactions occur with sulfur-centred radical addition to the C=C double bond of an alkene (Propagation reaction), followed by hydrogen abstraction from a thiol (Chain transfer reaction) which produces the other sulfur-centred radical (Figure 1.). It is especially important that radical step growth mechanism depends on both reactions and overall reaction order is related with the ratio of these reactions rate constants ( $k_P/k_{CT}$ ). Although thiol-ene reaction has been utilized in multiple of areas in materials and bioorganic chemistry, the extraordinary reactivity and stability of the sulfur-centred radicals have yet to be fully accounted for. This study focuses on the structure-reactivity relationships of thiyl radical addition reaction<sup>2,3</sup> in order to clarify one of the fundamental steps of thiol-ene reaction mechanism. In addition to this, the reactivity and stability of thiyl radicals in radical addition toward alkenes, thioketones, and thioesters are elaborated with high-level ab initio calculations. The extraordinary rapid addition reactions of thiyl radicals have been explained by the aid of G3(MP2)-RAD//MP2/6-31G(d) composite method calculations on a series of model reactions. High the SOMO energy of the radical allows better resonance interactions with  $\pi^*$  of the substrate, leading to earlier stabilization of the product configuration and hence an earlier and more stable transition state. For the same reason, we also find that thiyl radicals tend to be stabilized to a greater extent by heavier lone-pair donor and  $\pi$ -acceptor substituents, compared with their carbon-centred radical counterparts.



**Figure 1.** Radical thiol-ene reaction mechanism.

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## P31-Modeling of human GluNR<sub>1</sub>-GluNR<sub>2A</sub> NMDA receptor

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The structural differences of two recently solved X-Ray structures of NMDA type glutamate receptors, (Karakas and Furukawa: *Science* 344, 992 (2014) and Lee et al.: *Nature* 511,191 (2014)) are analysed. Homology model of the human heterotetrameric NMDA receptor is modelled based on the template structures. Loops missing in between extracellular, amino terminal and transmembrane domains are built by ab-initio folding by using Rosetta loop modeling program. Elastic network analysis has been carried out and a set of structural ruler type parameters are developed to monitor the conformational change of individual normal modes in a systematic way.

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## P32-X-ray diffraction studies of Ni(II) complex derived from 3,4-diaminobenzophenone

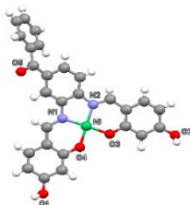
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Benzophenone has been the object of many spectral, structural and theoretical investigations because of its interesting chemical and physical properties. Further, the crystals of benzophenones are found to be useful materials for the fabrication of non-linear optical devices [1]. Moreover, Schiff base metal complexes containing different metal ions such as Ni, Co, Cu, Mn and Fe have been studied in great details for their various crystallographic features, structure–redox relationships and enzymatic reactions, mesogenic characteristics and catalytic properties. A considerable number of Schiff-base complexes have potential biological interest and are used as more or less successful models of biological compounds. Additionally, some of the salicylidene derivatives show photochromism in the solid state most likely due to intramolecular proton transfer associated with either a change in  $\pi$ -electron configuration or isomerization in the non-planar molecule [2].

In the first step of our study, ONNO donor diimine ligand, 2,4-dihydroxy salisiliden-3,4-diaminobenzophenone, was obtained by the reaction of 3,4-diaminobenzophenone with 2,4-dihydroxybenzaldehyde in the ethanol. In the second step, metal complexes of ligand was synthesized by using Ni(II) metal salts. Single crystals were obtained by slow evaporation of a ethanol-DKM mixture solution of the product. A red rod-like specimen of  $C_{27}H_{18}N_2NiO_5$  was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 VENTURE system equipped with a multilayer monochromator and a Mo  $K\alpha$  Sealed tube ( $\lambda = 0.71073 \text{ \AA}$ ).



**Figure 1:** ORTEP diagram of the complex.

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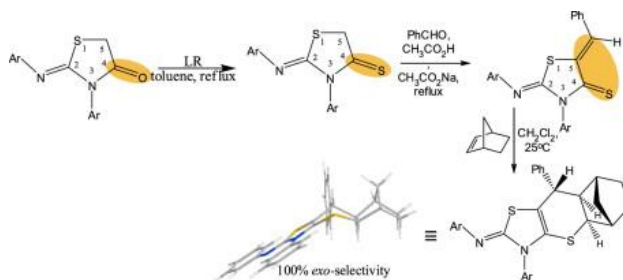
## P33-Exo-Selective inverse-electron-demand hetero Diels–Alder reactions of norbornene with 5-benzylidene-2-arylimino-3-aryl-thiazolidine-4-thiones

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2-Arylimino-3-aryl-thiazolidine-4-thiones were synthesized from the corresponding thiazolidine-4-ones using Lawesson's reagent (LR) and converted into 5-benzylidene-2-arylimino-3-aryl-thiazolidine-4-thiones by reaction with benzaldehyde, which were then used as heterodienes in the inverse electron-demand hetero Diels-Alder cycloadditions with norbornene as a dienophile.<sup>1</sup> The reactions with norbornene were found to proceed with 100% *exo*-selectivity. The *exo* selectivity in the reaction was investigated with computational tools.<sup>2</sup> Computational results are consistent with the experimental results.



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## P34-Crystallographic studies of dioxomolybdenum(VI) complex

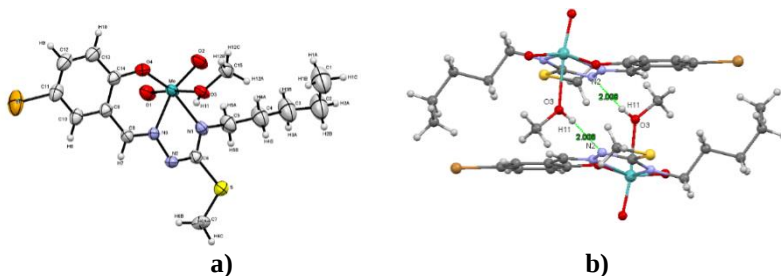
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Thiosemicarbazone metal complexes have raised considerable interest due to their wide range of biological activities (1). The molybdenum complexes of thiosemicarbazones are potential enzyme catalysts in which the catalytic capacity is thought to be related to the structural features of the chelated cis-MoO<sub>2</sub><sup>2+</sup> core (2).

Herein, we present the single crystal X-ray diffraction studies of methanol solvated dioxomolybdenum(VI) complex of N<sup>4</sup>-pentyl-S-methyl thiosemicarbazone having ONN donor set. Complex crystallizes in monoclinic crystal system with P 21/c space group symmetry. In the complex molecule, the thiosemicarbazone ligand is coordinated to dioxomolybdenum(VI) center via phenolic oxygen, azomethine nitrogen and thioamide nitrogen atoms (Figure 1). Considering the bond distance and angle values, the coordination sphere of the complex can be described as distorted octahedral geometry. In the crystal structure, two dioxomolybdenum complexes connect to the each other via N2·····H11-O3 hydrogen bond, so forming together a centrosymmetric dimer.



**Figure 1.** ORTEP diagram (a) and intermolecular interactions (b) of the complex.

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## P35-Virtual screening of approved drugs for pyruvate kinase inhibition of antibiotic-resistant bacteria

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Pyruvate kinase is a hub protein which catalyzes the last step of glycolysis. It is an attractive drug target because of distinct allosteric mechanisms in humans and bacteria. In this work, docking-based virtual screening is performed for three different conformers (PDB ID: 3t0t, 3t05, 3t07) of pyruvate kinase of methicillin-resistant *Staphylococcus aureus* (MRSA) using approved drugs. The screening focuses on a binding pocket at the interface of the tetrameric enzyme, to which several small molecule inhibitors have been previously shown to bind selectively in MRSA over humans <sup>[1]</sup>. For the screening, flexible docking was carried out for over 1900 approved drugs using Autodock v4 <sup>[2]</sup>. After analyzing the docking scores, top inhibitors that are common in all three conformers are determined. Top drugs include an Nebivolol which is an anti-hypertensive drug and Carminomycin which is an antibacterial and antitumor drug.

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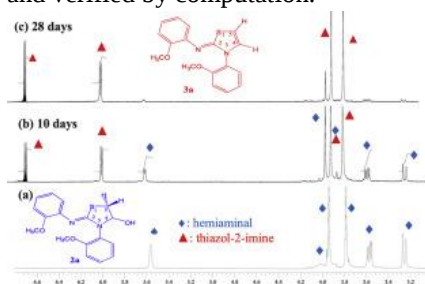
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# P36-Synthesis of stable tetrahedral intermediates (hemiaminals) and kinetics of their conversion to thiazol-2-imines

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Tetrahedral intermediates (hemiaminals) during thiazol-2-imine formation reactions have been isolated as stable compounds from the  $\text{LiAlH}_4$  reduction of the corresponding 2-arylimino-3-aryl-thiazolidine-4-ones.<sup>1</sup> In solution, the hemiaminals have been found to slowly convert to the corresponding thiazol-2-imines over time. The first order rate constants for the conversion processes have been determined by time dependent  $^1\text{H}$  NMR spectroscopic analyses. The stabilities of the hemiaminals were due to the amidine conjugation of the hemiaminal nitrogen and an intramolecular H-bonding interaction for the *o*-methoxyphenyl derivative as verified by computational studies. The reaction mechanism was investigated by DFT/M06-2X/6-31+G(d,p) method. The computational and experimental data are in agreement with an acid catalysed water elimination mechanism for the conversion of hemiaminal to thiazol-2-imine. Axial chirality of the hemiaminal 2-*o*-methoxyphenylimino-3-*o*-methoxyphenyl-thiazolidine-4-ol was modeled in DMF and in chloroform with DFT/M06-2X/6-31+G(d,p) method. Interestingly, a solvent induced conformational switching between P and M atropisomers has been observed by means of 2D NOESY and verified by computation.



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## P37-Theoretical investigation of thiol-ene click reactions: a DFT perspective

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In this study, for the first time a detailed study about the contribution of the phenyl thiol derivatives on the thiol-ene reaction mechanism has been carried out by using quantum chemical tools. DFT calculations have been used to investigate substitution effect on eleven thiol-ene reactions. It is well known that the reaction mechanism is strongly controlled by the  $k_p/k_{CT}$  ratio, where  $k_p$  is the propagation rate constant of the thyl addition to the alkene and  $k_{CT}$  is the rate constant of chain transfer to a thiol. All geometry optimizations and rate coefficients have been carried out with the M06-2X/6-31++G(d,p) methodology. The electrophilic nature of the phenylthio radicals and the S-T gap of the alkenes are mainly responsible for variation of the activation barriers of the propagation reaction, this demonstrates the importance of the ene functionality on the propagation reaction. The transition structures of the chain transfer reactions are stabilized by intramolecular interactions which lower the activation barriers. This study has revealed the fact that the  $k_p/k_{CT}$  ratio for the thiol-ene reactions does not only depend on the alkene functionality but on the thiol functionality as well, tailor-made polymers can be obtained by altering the substituents and the computational procedure described herein will guide the synthesis.

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# P38-Catalytic activity of Au(210) surface for sodium and lithium borohydride hydrolysis reaction: a DFT study

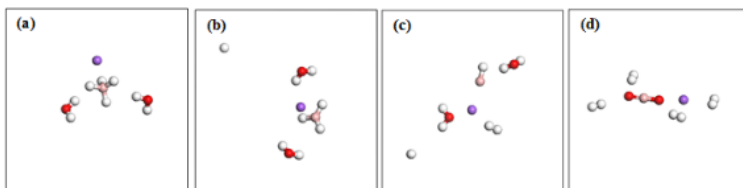
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The usage of hydrogen on mobile applications have been very popular since decades due to the possible energy crisis in near future because of depleting fossil fuel resources. Hydrogen is the first candidate over the carbon-based fossil fuels. In order to replace fossil fuels, effective usage of hydrogen should be established for daily utilization. Until now, high-pressurized tanks, cryogenic liquefaction have been investigated; However they did not meet the expectations[1]. However, these systems exhibit some drawbacks such as pressure control, bulky structure and leakage. Also, molecular hydrogen can be stored in carbon nanotubes[2], Metal-Organic Frameworks[3], Graphene[4] via Van der Waals interactions. Instead of these systems, spontaneous generation and instantaneous usage of hydrogen can be considered. Sodium (SB) and Lithium Borohydride (LB) has been taken much interest because it serves safe and spontaneous hydrogen evolution with the water at room temperature. SB and LB have 10.8 %wt and 18.4 %wt gravimetric hydrogen capacity, respectively, environmental friendly hydrolysis product ( $\text{NaBO}_2$ ,  $\text{LiBO}_2$ ), low reaction temperature [5,6].



**Figure 1.** (a) The reactant Configuration :  $\text{NaBH}_4 + 2\text{H}_2\text{O}$ , (b) Reaction Intermediate:  $\text{NaBH}_3 + \text{H} + 2\text{H}_2\text{O}$ , (c) Transition State:  $\text{NaBH} + \text{H} + 2\text{OH} + 2\text{H}_2$ , (d) Product:  $\text{NaBO}_2 + 4\text{H}_2$ . The purple, white, pink and red spheres stand for Sodium, Hydrogen, Boron and Oxygen atoms, respectively.

SB and LB have chemically bonded hydrogen to the  $[\text{BH}_4]^-$  group can be also abstracted by catalysts with a high efficiency than uncatalyzed medium. It is very important point that there is no consensus about certain reaction mechanism

along with the effect of the pH concentration for both catalytic and non-catalytic medium. In this work, catalytic activity of Au(210) single-crystal surface for SB and LB hydrolysis reaction are determined. Reaction mechanism is updated from the article of Janik et al. [7] and modified to have free OH<sup>-</sup> (Hydroxyl) ions to show the effect of the pH concentration to the activation barrier. Catalytic activity of these surfaces are determined via relative energy differences given by,

$$E_{Relative} = E_{All\ steps} - E_{Reactant}$$

Calculations are carried out via CASTEP simulation package which is based on Density Functional Theory. The exchange-correlation term is calculated by PW91 within generalized gradient approximation (GGA) [8]. Catalytic activity of Au(210) single-crystal surface for SB and LB hydrolysis reaction are obtained and compared with the non-catalytic medium.

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# **P39-Mutations affecting communication of residues disclose residues of evolutionary relevance**

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Network approach is utilized to investigate the structural changes occurring through point mutations. These changes may be correlated with the evolutionary roles of amino acids. We perform computational alanine scanning on a non-homologous set of 40 proteins using the recipe outlined previously [1]. To construct a residue network, we assign a node to the  $C_{\beta}$  atom of each residue and assign an edge between the nodes which are within the first coordination shell of each other. We inspect the changes in the mutant networks by using the shortest path length ( $L$ ), betweenness centrality (BC), neighbor count ( $k$ ) and clustering coefficient ( $C$ ) of the nodes with respect to the wild-type as the measures [2], [3]. We then relate the results averaged over all mutants to their conservation scores [4]. As a case study, bacterial enzyme dihydrofolate reductase (DHFR, pdb id: 1rx2) is selected for its significance as a model system for studying antibiotic resistance [5], [6]. The apo and holo DHFR structures are studied to delineate the effect of ligands. We observe  $k$  and BC as the parameters that best describe the difference between two forms, in alignment with our results from the 40 protein test set. In particular, residues I5, A6, V99 and Y151 display high BC values that signify structural importance in DHFR. Our results reveal the evolutionary importance and the structural significance of point mutations in proteins through mutational perturbations.

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## **P40-Discovery of cryptochrome destabilizer small molecules enhancing the apoptosis**

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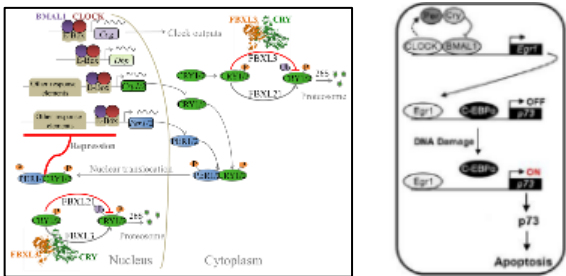
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Circadian rhythm controls the behavioral, biochemical and physical activities of the organisms in which they are found from cyanobacteria to human. Although this rhythm is endogenous, environmental and social factors entrain the rhythm to align its phase exactly to 24-hours via circadian clock mechanism. Circadian clock in mammals is located in the suprachiasmatic nuclei (SCN), synchronizes all clocks located in tissues via hormones and neuronal signals. Clock mechanism is controlled by two interconnected transcription/translation feedback loops (TTFL) at the molecular level. Four integral clock proteins drive the clock. These are two activators (BMAL1 and CLOCK) and two repressors (PER and CRY). BMAL1-CLOCK forms the dimer and binds to E-box in the promoter region of genes (~40% of all genes) including *Cry* and *Per* (positive arm of the TTFL). PER and CRY proteins accumulate in the cytoplasm and translocate to nucleus to inhibit BMAL1-CLOCK driven transactivation (negative arm of the TTFL)[1] (Figure 1a). Impairment of the organism's clock increases the susceptibility to various diseases, for example depression, jetlag, sleep disorders, neurological and cardiovascular diseases, cancer, diabetes and obesity. Furthermore, it has been shown that loss of CRY in cancer prone mice (p53<sup>-/-</sup>), unexpectedly, caused longer life span than cancer prone mice having the CRY, by initiating the apoptosis through upregulation of p73 [2, 3] (Figure 1b). The SCF-FBXL3 and FBXL21 ubiquitin ligase complexes act antagonistically and mediate the degradation of the CRY (Figure 1a). The recent study revealed co-crystal structure of the FBXL3 and CRY2, and showed that FBXL3 interacts with CRY through Flavin binding pocket [4]. On the other hand, biochemical analysis showed that FBXL21 interacts critically through pocket2 of CRY [5, 6]. Since small molecules are very useful tool to modulate protein-protein

interaction we aimed to identify small molecules by taking advantage of the docking simulations targeting the FBXL3 or FBXL21 binding pocket of CRY to decrease the overall CRY stability thereby to enhance the apoptosis.

After screening more than 1.5million small molecules *in silico* by using the Autodock Vina and testing 150 molecules experimentally, we identified 29 molecules modulating the half-life of CRY. Among those one molecule (M47) was well characterized. It has been shown that M47 treatment decreased the CRY level thus increased the transactivation of BMAL1:CLOCK both in U2OS cell lines and in C57BL/6 mice, and enhanced apoptosis after oxaliplatin treatment in MEF cell lines.



a)  
b)  
**Figure 1:** a) Mechanism of circadian clock and control of CRY stability. b) Mechanism of

apoptosis initiation as a result of decrease in CRY.

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# P41-Computational study of N-acetylneuraminic acid tryptophan interactions

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In this project, we studied conformational analysis of the  $\beta$ -form of N-acetylneuraminic acid, which is a kind of sialic acid, is quite dominant in mammals and the most stable structures were studied with tryptophan interactions.

Sialic acid is a sugar contains an amino group, acetylated derivatives of sialic acid are found in glycoproteins and glycolipids of plasma membranes and other cellular components. In this study, N-acetylneuraminic acid (NANA) was selected for ganglioside structures on the cell surface of tumor cells<sup>1-3</sup>. The structural forms of NANA are  $\alpha$  form and  $\beta$  form. The beta form was selected for this study because it is dominant in living systems.

Lectins can specifically bind to sugars, found in such as plants, animals, viruses. In lectin structure, there are certain amino acids in the binding regions of the protein that interact with the cell surface. One of these amino acid is tryptophan, which has an aromatic group<sup>4</sup>.

The  $\beta$  form of N-acetylneuraminic acid was calculated by Spartan'16 with conformer distribution molecular mechanics/MMFF options. 985 possible conformers were found. These conformers were investigated by Density Functional Theory (DFT) in the Gaussian09 program. The DFT calculation was applied  $\omega$ B97xD/6-31G (d, p) level. Calculating the relative energies, the 4 most stable structures were re-optimized in the upper basis set, 6-311G++(d,p). Conformational analysis were performed using SYBYL force field as implemented in Spartan'16 software in order to generate input structures which includes 4 structures of NANA and optimized tryptophan complexes. In conclusion, NANA-Tryptophan complexes were optimized in an aqueous environment by using PCM and all these calculations were carried out by DFT in Gaussian09.

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# P42-3-Bromo-5-chloro-2-hydroxyacetophenone-N<sup>4</sup>-butyl-thiosemicarbazidato triphenylphosphine palladium(II) complex

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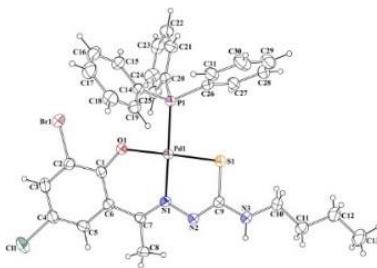
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Thiosemicarbazones represent an important class of Schiff base ligands having sulphur and nitrogen as donor atoms. Thiosemicarbazones and their transition metal complexes have a wide range of pharmacological properties such as antimicrobial, antitumor and antiviral activity [1, 2]. In addition, palladium(II) thiosemicarbazones possess interesting antiproliferative effects on human cancer cell lines [3, 4].

In this study, the reaction of 3-bromo-5-chloro-2-hydroxyacetophenone-N<sup>4</sup>-butyl-thiosemicarbazone with an equimolar amount of Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> has afforded [PdL(PPh<sub>3</sub>)] complex. Thiosemicarbazone ligand and palladium(II) phosphine complex was characterized by elemental analysis, IR and <sup>1</sup>H-NMR spectrum and the complex was also determined by single crystal X-ray diffraction.



[PdL(PPh<sub>3</sub>)] complex

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## P43-Nickel(II) complex based on thiosemicarbazone: crystallographic, spectroscopic and DFT calculations

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Thiosemicarbazones constitute a class of ligand that presents considerable interest to structural and medicinal chemists, because of their therapeutic potential [1, 2]. Their properties change depending on metal atom, coordination modes, connected aldehyde or ketone and substituents on aldehyde/ ketone [3, 4] The square-planar complex of Ni(II) with condensation derivative of 2-hydroxyacetophenone and S-propyl-4-methyl-thiosemicarbazide have been synthesized and characterized on the basis of the results of X-Ray, NMR and IR spectroscopy and elemental analysis. In addition, the molecular geometries, vibrational frequencies have been calculated using the density functional theory B3LYP and M06-2X functional was tested against the crystal structure data with LANL2DZ for the Ni atom and 6-31+G(d) for the other atoms.

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# P44-Nano-hemoglobin film based sextet state biomemory device by cross-linked photosensitive hapten monomer

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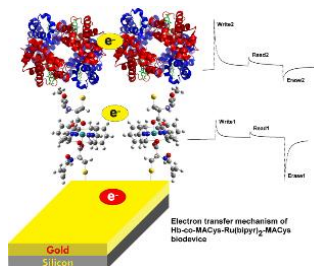
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The metalloproteins that provide electron transfer in biological system have high importance among the biomolecules. Thus, due to providing appropriate circumstances to saturate the electrons, the metalloproteins can be used to develop bioelectronic device<sup>[1,2]</sup>.

In this study, a biomemory device, consisting of hemoglobin (Hb) cross-linked by MACys-Ru(bipyridine)<sub>2</sub>-MACys photosensitive monomer cross-linkers, which have memory effect through both Ru<sup>3+/2+</sup> in hapten monomer and Fe<sup>3+/2+</sup> in redox active center of Hb through multi-charge transfer mechanism, has been improved (Figure 1). Cyclic voltammetry (CV) has been used to determine the redox property of the Hb cross-linked MACys-Ru(bipyridine)<sub>2</sub>-MACys hapten. Three memory functions, writing, reading and erasing of the fabricated biomemory device, have been accomplished by chronoamperometry (CA) and open-circuit potential amperometry (OCPA). The reliability and repetability of the biodevice consisting of the p(Hb-co-MACys-Ru(bipyridine)<sub>2</sub>-MACys) sextet state bio-memory layer have been analysed. The Hb film based biodevice on gold electrodes has shown  $\geq 2$  months the retention time and switched until 10<sup>6</sup> times continuous



cycling without degradation in efficiency.

**Figure 1.** The charge transfer process for Hb/MACys-Ru(bipyridine)<sub>2</sub>-MACys) memory device

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## P45-Elucidation of atroposelective synthesis of axially chiral thiohydantoin derivatives

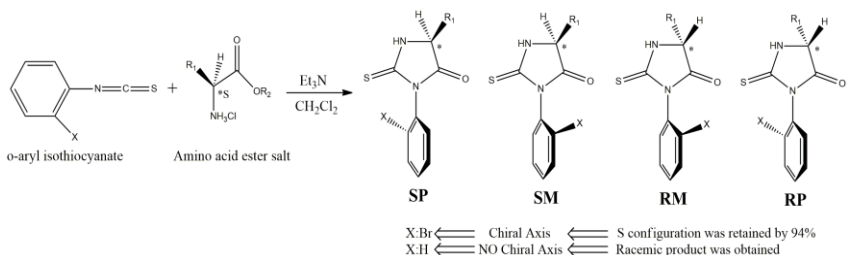
Z. P. Haşlak<sup>1,2</sup>, S. Çınar<sup>1</sup>, S. Sarıgül<sup>1</sup>, İ. Doğan<sup>1</sup>, V. Aviyente<sup>1</sup>

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Hydantoins, a class of cyclic imides, have broad range of biological and agricultural activities. Hydantoin derivatives are also important precursors in the synthesis of several aminoacids and pyruvic acid derivatives due to the diversity of the synthetic methods for the modification of the exocyclic double bond [1]. Chirality of a drug molecule is known to have an effect on its pharmacological activity. Due to the importance of these compounds, some of us have synthesized axially chiral derivatives of thiohydantoin (**RM-SM-RP-SP**) and have observed the interconversion of **S** and **R** stereoisomers [2]. In this study, DFT calculations have been used in order to understand the mechanism of synthesis, chirality transfer and interconversion of the stereoisomers. For this purpose, mechanistic details are investigated by making use of the M06-2X/6-311+G\*\* methodology and the explicit solvent model is applied in order to mimic the reaction environment.



**Figure 1.** Synthesis of thiohydantoin derivatives.

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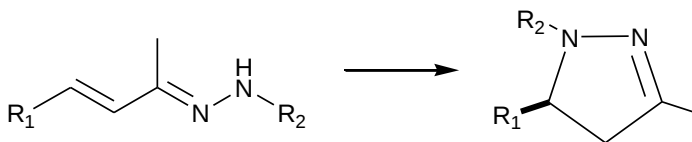
## P46-Mechanistic aspects of catalytic asymmetric $6\pi$ -electrocyclization: a DFT study

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Pericyclic reactions are of utmost significance in synthetic organic chemistry, owing to their synthetic feasibility.<sup>1</sup> In a recent study, Müller et al. experimentally investigated  $6\pi$ -electrocyclization of  $\alpha,\beta$ -unsaturated hydrazones and the products of 2-pyrazolines (Scheme 1).<sup>2</sup> In the present study, the reaction modes of two different models have been investigated by means of Density Functional Theory (DFT) calculations. To reveal whether a pericyclic-like mechanism or intramolecular Michael addition-like fashion is more feasible for pyrazolines, reaction profiles have been constructed, as well as different population schemes and molecular orbital coefficients have been thoroughly analyzed. Effects of solvation and non-covalent interactions have been included.



**Scheme 1.**  $6\pi$ -electrocyclization of  $\alpha,\beta$ -unsaturated hydrazones.

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## P47-Predicting self-assembly of nanoparticles for targeted drug delivery

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The balance between solubility and membrane permeability contributes to dosage limits of cancer drugs. Some poorly soluble kinase inhibitors can form nanoparticles spontaneously when mixed with specific molecules. These inactive molecules can serve as excipients for making targeted nanomedicines with very high drug loadings(90% by mass) and high blood stability. These nanoparticles were shown to specifically target delivery of kinase inhibitors to certain tumours, reducing on- and off-target toxicities.

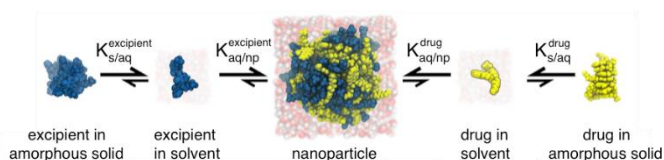


Figure 1. Thermodynamic scheme for formation of drug-excipient nanoparticle.

To predict which drugs can form nanoparticles with excipients, utility of cheminformatics based methods and molecular dynamics of the nucleation stage were investigated. With quantitative structure-nanoparticle assembly prediction (QSNAP) calculations based on available experimental data, we identified electrotopological molecular descriptors –which correlate with presence of electronegative groups– as highly predictive indicators of nanoparticle formation. Some drug-excipient nanoparticles tested *in vivo* showed selective targeted delivery of kinase inhibitors to caveolin-1-expressing human colon cancer and autochthonous liver cancer models to yield striking therapeutic effects while avoiding side effects in healthy skin.<sup>1</sup>

On-going work is focused on elucidating the mechanisms controlling self-assembly. We are predicting phase-transfer free energies of nanoparticle

components to test hypotheses about thermodynamically-driven nanoparticle assembly and stability using free energy methods.

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## **P48-Developing doxycycline imprinted hydrogels using computational and experimental approaches**

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Molecular imprinting is a technique used to enable recognition of small molecules by creating their corresponding template-shaped cavities in polymer matrices. This technique is employed in many applications such as diagnosis, biosensors, bioseparation, and particularly in controlled drug delivery systems [1]. Interactions between monomers and the target molecule [2] and concentration of the crosslinker [3] prior to polymerization are the main factors that affect molecular recognition and drug release performance of a molecularly imprinted polymer.

This study aims to develop antibiotic doxycycline imprinted hydrogels, that can find various applications in the treatment of different infections. For this purpose, the study takes both computational and experimental approaches. The computational approach includes simulated annealing and molecular dynamic (MD) simulations using Materials Studio v8.0. In simulated annealing studies, reaction media containing hydroxyethyl methacrylate – HEMA (main chain monomer), ethylene glycol dimethacrylate – EGDMA (crosslinker), doxycycline – DOX (template molecule) and functional monomers (acrylic acid – AA, itaconic acid – IA or methacrylic acid – MAA) were simulated to determine an effective functional monomer for the imprinting process by analyzing monomer – template interactions. Simulated annealing procedure followed a temperature increase from 298 K to 498 K and cooling to 298 K, gradually. The heating – cooling process was carried out in a total of 25 cycles for 1 ns including 106 steps.

Guided by the simulated annealing simulations, in the experimental part, DOX drug molecules were imprinted on functional monomer AA-based hydrogel

matrices by free radical polymerization using EGDMA. Different EGDMA ratios (1, 1.5, 2, 3 mole%) were investigated to understand the effect of the cross-linker concentration on drug loading and release performances of the hydrogels. Release data were evaluated by zero-order, first-order, Higuchi and Korsmeyer Peppas models to understand release kinetics. Drugs were also loaded to hydrogels by soaking method for comparison. In order to interpret the experimental results on different EGDMA ratios, 5 ns long MD simulations of the cross-linker, DOX and AA system were performed under periodic boundary conditions, with NVT ensemble at 298 K.

According to results, simulated annealing studies show that IA and AA functional monomers make more stable complexes with DOX as compared to MAA. All experimental results on imprinted, non-imprinted hydrogels as well as MD simulations indicate that imprinting is more efficient when EGDMA ratio is 3%, therefore these hydrogels show the most controlled DOXH release. This result is supported by kinetic drug release models.

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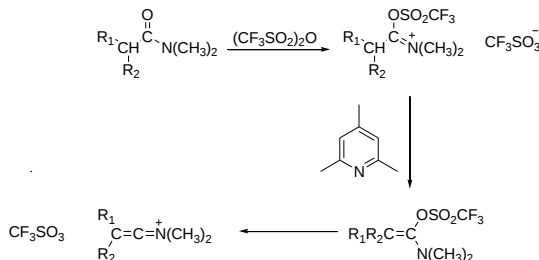
## P49-A computational study on the formation of keteniminium salts

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Keteniminium salts are generally an improved alternative to their ketene analogues due to their higher electrophilicity and reactivity properties. Keteniminium salts do not dimerize or polymerize as readily as ketenes, therefore they provide a higher electrophilic reactivity while avoiding some unwanted side reactions that may lead to their destruction.<sup>1</sup> This study aims to computationally rationalize the formation of keteniminium salts by using a DFT approach. In this regard, we elucidate four different paths to keteniminium salt formation including, protonation of ynamines and ynamides,<sup>2</sup> alkylation of corresponding ketenimines<sup>3</sup> and the reaction of  $\alpha$ -halo enamines with Lewis acids<sup>4</sup> as well as Ghosez's mechanism for keteniminium salt formation.<sup>5</sup> These different pathways are modelled and compared to one another in order to find the most probable mechanism for the formation of the keteniminium salts.



**Scheme 1.** Ghosez's Mechanism for the Formation of Keteniminium Salts<sup>5</sup>

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# P50-X-ray crystallographic studies of bisthiocarbohydrazone ligand derived from 2-hydroxy-4-methoxybenzophenone

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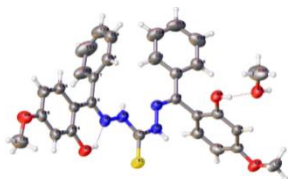
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Thiocarbohydrazone ( $\text{H}_2\text{N}-\text{NH}-(\text{C}=\text{S})-\text{NH}-\text{NH}_2$ ) is a promising unit to synthesize new polyfunctional organic compounds, named as thiocarbohydrazone after condensation with an aldehyde or ketone [1]. Thiocarbohydrazones, a class of compounds possessing a wide spectrum of medicinal properties, have been studied for activity against tuberculosis, cancer, bacterial and viral infections [2].

Benzophenone derivatives are very important compounds due to their various biological and physicochemical properties such as electrochemical, spectroscopic, metal complexation, adsorptive and crystallographic properties among others. The most important biological property of benzophenone derivatives is their ability to absorb a broad range of UV radiation (~200 to 350 nm). Due to this property, benzophenones were used as raw materials in the manufacture of sunscreen creams. These creams are helpful to avoid photosensitization, phototoxicity or allergic reactions of patients with various medicinal treatments [3].

Bisthiocarbohydrazone ligand was obtained by the condensation of thiocarbohydrazone with 2-hydroxy-4-methoxybenzophenone (1:2) in ethanol. Light brown single crystals of the Schiff base were grown by slow evaporation of a methanolic solution over 7 days at room temperature, and its structure was determined by X-ray crystallography. A monoclinic system was proposed by X-ray powder diffraction study of Schiff base.



**Figure 1:** ORTEP diagram of the ligand.

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# P51-Square pyramidal iron(III) complex of an N<sub>2</sub>O<sub>2</sub>-chelating thiosemicarbazone with azide co-ligands

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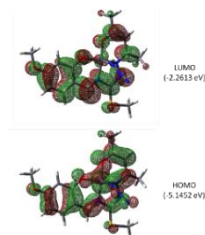
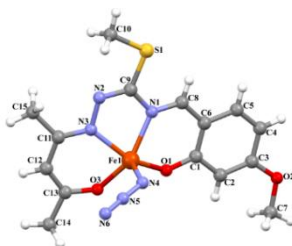
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Thiosemicarbazones derived carbonyl compounds are multidentate ligands. The derivatives condensed with two same or different hydroxy-carbonyl compounds are dibasic tetradentate thiosemicarbazidato ligands and these structures are convenient to form a square plane geometry around a transition metal ion<sup>1,2</sup>. When the center atom is iron(III), by the participation of a second ligand can be reached to a five coordinated complex molecule based on square pyramid model.



The report deals experimental and theoretical characterization of a mixed ligand iron(III) complex with N<sup>1</sup>-acetylacetone-N<sup>4</sup>-4-methoxysalicylidene-S-methyl-thiosemicarbazidato (L<sup>2-</sup>) and azide (N<sub>3</sub><sup>-</sup>) ligands. Structure of the potential biological active complex<sup>2</sup>, [FeL(N<sub>3</sub>)], was carried out by X-ray diffraction analysis. Theoretical characterization of the iron(III) complex was performed by B3LYP/3-21G\*method using density functional theory (DFT)<sup>3,4</sup>.

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## P52-The effect of cation doping on the electronic structure of TiO<sub>2</sub>

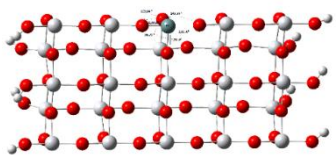
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TiO<sub>2</sub> is a promising photocatalyst for water and air purification, because it is chemically inert, photostable, inexpensive, nontoxic, and has high oxidative power. However, TiO<sub>2</sub> has a wide band-gap (~3.2 eV) and is only excited by UV-light, it is inactive under visible light irradiation. Thus, much of the research developed in recent years has been focused on extending the optical absorption of TiO<sub>2</sub> to the visible region of the spectrum in order to substitute UV-light by sunlight to make use of solar energy for practical applications. One way to achieve this is doping of impurities into the TiO<sub>2</sub> matrix in order to reduce the band gap. It has been known that doped cations, induce visible-light absorption and influence the photoreactivity of TiO<sub>2</sub>. Numerous cations have been investigated as potential dopants, however there is a considerable controversy in the results obtained for their effect. Despite extensive research on cation-doped TiO<sub>2</sub>, there is still no unifying result or explanation for the effect of cations on the photocatalytic activity of TiO<sub>2</sub> under solar light.



In this study, the non-defective anatase (001) surface was modeled with finite, neutral, stoichiometric cluster models cut from the anatase bulk structure, in order to determine the location and the bonding status of the

dopant cations. In the doped models, substitutional locations of cations were analyzed. The structures of the doped models were constructed by replacing one titanium atom by one cation. All the calculations were carried out using the Density Functional Theory DFT method. The DFT calculations were performed by the hybrid B3LYP functional. The double-zeta LanL2DZ basis set was used in order to take the relativistic effects into account. The dopant positions were optimized by changing their locations in the clusters to find the lowest energy configuration.

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## **P53-Computational assessment of allosteric mutations on the dynamics of pdz domains**

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Allostery is a biological phenomenon where perturbations at one site of the protein, such as due to binding, can influence changes at a distal site, complicating deducing structure-function relationship in proteins<sup>1</sup>. PDZ domains are commonly employed for interpreting allosteric mechanisms<sup>2</sup>. Their domains consist of 90 to 100 amino acids and are responsible for various signaling pathways by identifying short C termini of target proteins<sup>3</sup>. Due to their well-defined binding sites, and their role in signaling pathways, they are therapeutic targets in neurological disorders<sup>4</sup>. By using third PDZ domain of postsynaptic density 95 (PSD-95) as a model system, two different amino acids, H372 directly connected to the binding site and G330 with a somewhat removed position, were selected to assess the structural features of the PDZ domain and effect of allosteric mutations on the dynamics<sup>5</sup>. It was observed that the H372A and G330T/H372A mutations change ligand preferences from class I (T/S residue preference at position 2 of the ligand) to class II (hydrophobic amino acid preference at position 2 of the ligand). On the other hand, the G330T mutation leads to the recognition of both class I and class II types of ligands. Therefore, H372A is a ‘switching mutation’ while G330T mutation is ‘class bridging’. We have performed 200 ns molecular dynamics simulations for wild type, H372A, G330T single mutants and double mutant of third PDZ domain in the absence and presence of both types of ligands. Preliminary results show a strong control over the N-terminus fluctuations depending on the mutation type and absence/presence of a ligand. In addition, occupancies for hydrogen bonds established between the ligand and PSD-95 help identify how the interaction between ligand and PSD-95 is affected by each mutation.

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## **P54-Design of donor-acceptor copolymers for organic photovoltaic materials: a computational study**

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80 different of push-pull type organic chromophores which possess Donor-Acceptor (D-A) and Donor-Thiophene-Donor-Thiophene (D-T-A-T) structures have been systematically investigated by means of the density functional theory (DFT) and time-dependent density functional theory (TD-DFT) at the B3LYP/6-311G\* level. The two different coupling typologies allow us to investigate the effect of  $\pi$ -spacer accurately.<sup>1</sup> The HOMO, LUMO energies and transition dipoles are seen to converge for tetrameric oligomers, the latter have been used as optimal chain length to evaluate various optical and geometrical properties such as reorganization energies, vertical excitation energies to lowest lying excited state, bond length alternations, distortion energies and frontier molecular.<sup>2</sup>

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## **P55-A study of rolling mechanism of single molecule on metal surface: DFT and molecular dynamic simulations**

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We present the results of DFT and molecular dynamic calculations for wheel dimer molecule on corrugated Cu(110) surface. We examined all possible configurations of  $C_{44}H_{26}$  with respect to substrate based on calculations with the vDW-D2 and PBE functional to compare with the experimental results and to better understand the role of van der Waals interactions on the adsorptions of wheel dimer molecule. We also performed molecular dynamic calculations to investigate how the temperature of the system plays roles on the configurations of the molecules on Cu(110) surface. . Furthermore, to identify the behavior of molecular motions on corrugated metal surface in the existence of STM tip, we looked deeper into the position of STM tip with respect to central molecular axle during the molecular dynamic simulations. Using the results of MD simulations in the existence of STM tip, we further discussed the position of STM tip for rolling mechanisms of wheel dimer molecule on Cu(110) surface.

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## **P56-On the development of molecular mechanics force field parameters**

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Molecular mechanics is a powerful and well-established method to study biomolecular systems with great number of atoms. Among others, one great advantage is its low computational cost, which stems from a formulation based on classical mechanics and parameterized equations. While parameters allow fast and accurate calculations to model the systems that they have been tailored to describe, molecular mechanics suffers a certain lack of generalizability. Many force fields have been developed and further improved over the past decades to model highly relevant macromolecular assemblies (e.g., proteins, membranes, ...). However, parameters are often missing for particular moieties, such as ligands or non-standard amino acids, and those need to be specifically optimized. Far from being exhaustive, this discussion presents some fundamental aspects of parameters development through illustrations from our recent work: from straight forward independent molecules to more complex polymeric assemblies.

# P57-Molecular dynamics and docking studies on the interactions of DNA with quaternary metallo phthalocyanines

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Owing to its central role of in replication and transcription, DNA has been a major target for antibiotic, anticancer, and antiviral drugs<sup>1</sup>. Cationic porphyrins are considered as functional compounds that strongly bind to DNA and photodynamically modify the target site of a DNA molecule by a mechanism similar to that of anticancer drugs<sup>2</sup>. On the other hand, despite spectrophotometric studies on the interactions of phthalocyanines (Pcs) with DNA are abundant<sup>3</sup>, molecular modelling studies have not yet been recorded in the literature to our knowledge. The aim of this study is to investigate the interactions between DNA segment d(CGCA3T3GCG) (PDB ID: 2DND) and metallo Pcs (M=Zn, Ni, Cu, Fe, Ca, Mg) and to direct future experimental studies. The structure of a quaternized ZnPc (Q-ZnPc) synthesized previously and additional Q-MPcs were optimized with DFT/wb97xd/6-31G(d,p). A 20 ns Molecular Dynamics simulation was carried out on DNA using GROMACS 5.1.2 package and AMBER99 force-field. All the Q-MPcs were docked to the relaxed DNA segment using Autodock Vina and binding modes/sites were investigated (Fig. 1). Boltzmann averaged-docking scores were also calculated. The calculated Kb is in the agreement with the experimental value. Regarding the general trend among all the Q-MPcs, Boltzmann-averaged Kb values show much better agreement to the experimental value. Quaternary amine groups and metals improve binding affinity.

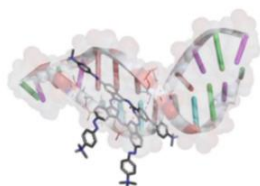


Fig. 1. Binding mode of Q-ZnPc

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## P58-The efficient cyclopolymerization of silyl-tethered styrenic difunctional monomers

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One of the main theme in modern polymer science is the accurate control over the sequence of monomeric units and their connections. Recently, some new strategies have been developed for controlling sequences in order to obtain fast and large-scale synthesis of polymers.<sup>[1]</sup> This study is related to cyclopolymerization which is a synthetic process for obtaining polymers with a controlled sequence of monomers forming cyclic structure on the polymer backbone by a mechanism of cyclization-propagation of difunctional monomers. The synthesis of styrenic difunctional monomers consist of the tethering of two polymerizable aromatic molecules by a covalent bond to a linking group for promoting the cyclization-propagation mechanism of cyclopolymerization. Usually the linking group is also a sterically hindered system.[2]

In the experimental work malonate ester was chosen as the tethering group. Despite of its simplicity this molecule has shown an efficient cyclopolymerization. Then, two different silanes: the dichlorodiphenylsilane and the dichloro(methyl)phenylsilane were chosen because of their low cost, their easy availability and because they should be removed after the cyclopolymerization as a common protecting group.<sup>[3]</sup>

In this work the synthesis and the efficient cyclopolymerization of difunctional monomers containing styrenic moieties tethered each other by different types of protecting groups were illustrated both experimentally and theoretically. Modelling studies were done by using M06-2X functional<sup>4</sup> along with the double zeta basis set 6-31G\* . All calculations have been performed with Gaussian 09 software package.<sup>5</sup>

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## **P59-Oncogenic mutations on Rac1 regulate Rac1-PAK1 binding by shifting the binding state through global mode perturbations**

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Ras-related C3 botulinum toxin substrate 1 (Rac1) is a small member of Rho GTPase family involved in regulation of many biological processes through acting as a binary switch between active and inactive states. One of the most important downstream effectors of Rac1 is p21-activated kinase 1 (PAK1), which is a serine/threonine kinase. Mutational activation of PAK1 by Rac1 was shown to have oncogenic signaling effects at various steps such as cell proliferation, survival, invasion and metastasis. Here, the Rac1-PAK1 interaction is explored by Single Molecule Force Spectroscopy (SMFS) experiments using Atomic Force Microscopy (AFM) as well as molecular dynamics simulations with elastic network model analysis and molecular docking to understand the dynamic regulation of the PAK1's binding behavior through mutations in Rac1. In this framework, the effects of the dominant-negative T17N, constitutively active Q61L and oncogenic Y72C mutations on the unbinding free energy landscape (FEL) of the Rac1-PAK1 dissociation reaction are explored using SMSF. The SMFS results indicate that the dissociation of GTP loaded wild-type Rac1-PAK1 complex follows two different pathways (so-called high and low-strength binding states) revealed by bimodal distribution of unbinding forces with two distinct dissociation rates. Q61L and Y72C mutations reduce the

number of pathways to one, with similar unbinding rate to the high strength binding state of the wild-type Rac1. On the other hand, Molecular Dynamics (MD) simulations of the wild-type Rac1 and Q61L and Y72C as well as two more oncogenic mutants P29S and Q61R indicates that there is a shift in the ensemble of conformations such that the cooperativity of residue fluctuations change with respect to the GEF, GAP and PAK1 binding sites. The association of these mutation sites with the global hinges of Rac1 explains the allosterically regulated interplay between the functional regions such as p-loop, switch and insert on Rac1, and rationalize the dynamic coupling between the mutations on these residues with the Rac1-PAK1 binding.

## **P60-Towards “synthetic metals” with acceptor-donor type conducting polymers**

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In this computational study, the band gap energy of an acceptor-donor type conducting polymer consisting of terthiophene repeating units with fused bisfulleroid group was estimated by extrapolating excitation energies approximated by the HOMO-LUMO energy differences as well as the TDDFT method with respect to the inverse number of monomer units. Optimizations were performed both in vacuum and in o-dichloro benzene (as solvent) using the B3LYP and MPW1B95 functionals. The calculated optical band gap was found to be in good agreement with experimentally reported band gap in the literature [1]. However, different band gaps with different experimental techniques were reported in the referred experimental study for the same system. In order to understand the reasons behind this behavior, effects of the structural (inter- and intra-molecular stacking) and environmental (explicit and implicit solvation and acidic doping) factors on the absorption of the terthiophene monomer with fused bisfulleroid were investigated. Acid-doping was found to be very important in terms of the present system[2].

Acknowledgements. This work is supported by ITU-UYBHM Grant No. 10822009

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# P61-Computational investigation of the KMO catalysed reaction mechanism between L-Kyn and FAD

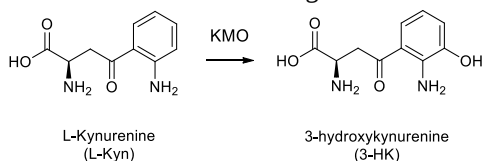
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A flavin adenine dinucleotide (FAD) dependent monooxygenase, kynurenine 3-monooxygenase (KMO), is located in the outer mitochondrial membrane where it converts L-kynurenine (L-Kyn) into 3-hydroxykynurenine (3-HK). This conversion is a part of kynurenine pathway (KP) in which tryptophan is catabolized to the final product nicotinamide adenine dinucleotide (NAD). Since the substrate of KMO, L-Kyn, corresponds to a branching point in KP, the activity of KMO has a regulatory function by means of controlling the levels of several metabolites. For example, abnormally high activity of KMO results in the overproduction of neurotoxic substance 3-HK<sup>1</sup>, whose overexpression is shown to be correlated with several diseases such as Parkinson's, Alzheimer's and Huntingtin's. Its abnormally lower activity on the other hand, paves the way for the overproduction of a normally neuroprotective substance, kynurenic acid (KynA), but again, whose overexpression is shown to be correlated with bipolar disorder and schizophrenia<sup>4</sup>.

Herein, especially focusing on the oxidative half reaction and the hydroxylation step, we present our quantum mechanical studies directed to elucidate the enzymatic reaction between L-Kyn and FAD. DFT calculations were carried out with both M06-L and B3LYP functionals alongside with 6-31+G(d,p) basis set.



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## P62-Allosteric control of the DNA-RNA translocation in telomerase

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The stabilization of the DNA-RNA duplex at the active site of telomerase during nucleotide incorporation and the mechanism of RNA-DNA translocation after the formation of the phosphodiester bond are not fully understood. To address these questions, *Tribolium castaneum* telomerase catalytic subunit TERT and the associated RNA-DNA hybrid have been simulated using Amber14 program with the ff14SB force field.

To investigate the structural changes along the functional cycle of telomerase, three different states have been modelled (without dNTP in the active site, with dNTP and after the incorporation of a nucleotide into the growing DNA chain). Each state can be considered as a step in the substrate recognition and translocation cycle.

In the crystal structure [1], dA23 of DNA is coordinated to RNA via Hoogsteen type hydrogen bonds. Such an interaction in telomerase is not expected, therefore all these three states have been investigated also by changing the conformation of this adenine in order to form a *canonical Watson-Crick* pair.

The analysis of these states has shown that before the formation of the phosphodiester bond between dNTP and DNA primer, TERT exhibits a closed conformation whereas after the formation of the phosphodiester bond, the fingers subdomain displays an opening movement. This opening movement is necessary for DNA-RNA translocation to allow further nucleotide addition. Some amino acid residues have critical roles in the allosteric control of opening. Therefore, they are mutated to alanine for testing their effect on the enzyme stabilization and allosteric regulation.

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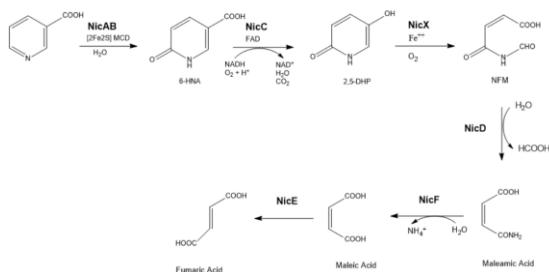
## P63-Action of nicc enzyme on nicotinate: a model DFT study

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N-heterocyclic aromatic compounds (NHACs) used in the construction of industrial materials cause contamination in groundwater and soil. Biodegradation of these compounds has been observed during redox reactions catalyzed by hydroxylase, monooxygenase and oxidoreductase enzymes. In these reactions, the organic substrate is oxidized to another molecule that is less harmful, and sometimes even more useful than itself. Nicotinic acid (NA, vitamin B3) is a model that can be used to study the chemical mechanisms of these compounds. From the Flavine-containing monooxygenase enzymes, NicC acts as a catalyst in the initiation mechanisms of these reactions. The aerobic degradation of nicotonic acid in *Pseudomonas fluorescens* bacteria by Behrman and Stanier is biochemically characterized (Figure 1). The hydroxylation and oxidation reactions convert pyridine, which is involved in the structures of the NHAC class compounds, to more benign metabolites. The 6-HNA, intermediate is a forebrain to subsequent degradation of nicotinate and it is converted to 2,5 DHP product in some aerobic bacteria in the presence of NicC catalyst. 2,5 DHP then contributes to the growth of organisms as a source of carbon and nitrogen by directing the formation of fumarate, formate and ammonia products. The main purpose of this study is investigate the NicC mechanism of this reactions chain in detail by quantum mechanical methods. The proposed two different paths are investigated by DFT calculations.<sup>1</sup>



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# P64-<sup>1</sup>H and <sup>13</sup>C NMR studies of 1,2,4,5-oxadiazaborole derivatives

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In medicinal chemistry, boron compounds have great potential in drug discovery. These compounds have been reported in the literature as having potential biological activities.<sup>1</sup> The chemical shifts in <sup>1</sup>H and <sup>13</sup>C NMR spectra are often used for the study of the transmission of substituent effects on molecules.

Substituent effects on <sup>1</sup>H and <sup>13</sup>C NMR chemical shifts of 3-substituted phenyl-4-(*m*-tolyl)-5-phenyl-4,5-dihydro-1,2,4,5-oxadiazaboroles (**1a-j**), 4-substituted phenyl-3-(*p*-chlorophenyl)-5-phenyl-4,5-dihydro-1,2,4,5-oxadiazaboroles (**2a-k**) and 5-substituted phenyl-3-phenyl-4,5-dihydro-1,2,4,5-oxadiazaboroles (**3a-r**) (Figure 1) were studied respectively. Single and dual substituent parameters were used for the correlation analysis of substituent-induced chemical shifts with  $\sigma$ ,  $F$  and  $R$  constants. The calculations have shown the polar and resonance substituent effects on N-H proton and C=N carbon atoms. The  $\rho$  values were found negative for both compounds (**1**) and (**2**), which means that the effect is reverse, however the  $\rho$  value for compounds (**3**) was positive, which shows the normal substituent effect. Density functional theory (DFT) calculations were carried out to calculate the theoretical chemical shifts, bond distances and bond angles.

The calculations for the geometry optimizations of compounds were done by DFT method on the basis of B3LYP exchange-correlation functional with 6-31G and 6-31++G(d,p) basis sets.

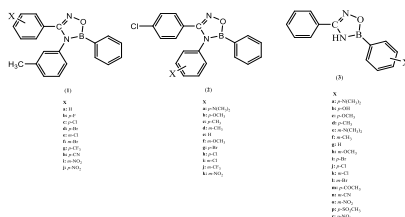


Figure 1. Structures of (**1a-j**), (**2a-k**) and (**3a-r**).

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## P65-Mechanistic dft study on the function of homoboroproline as asymmetric catalyst in enantioselective aldol reactions

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Chiral aminoboronic acids have a wide range of applications including anticancer agents, molecular sensors and especially as organic asymmetric catalysts<sup>1</sup>. Whiting's group<sup>2</sup> recently synthesized a new proline-based amino boronic acid (homoboroproline) and used it as an effective asymmetric catalyst in aldol reaction. The mechanism was assumed to follow the formation of enamine intermediate as in the case of other proline-based catalysts. However, contrary to proline catalyzed asymmetric aldol reaction, S-homoboroproline results in S-enantioselectivity. The purpose of this study is to investigate the mechanism and provide insight into the function of homoboroproline in enantioselective aldol reactions.

The reaction between aldehyde and the proposed enamine intermediate was modelled by DFT. All stationary points belonging to each step were optimized and characterized by PCM/M06-2X/6-31G(d,p) method in acetone solvent. Possible orientations of the enamine double bond and the addition of aldehyde from *re*- and *si*-faces were considered.

A theoretical model was proposed based on the cyclic transition state to explain the observed enantioselectivity: The stronger B-O interaction driven by the steric repulsion at the C-C forming bond was found to be important for the selectivity.

We acknowledge Marmara University Scientific Research Project Commission BAP for project no: FEN-B-100615-0269 and TUBITAK BİDEB 2210-C.

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## **P66-Molecular docking of arylcoumarins to carbapenemase enzyme**

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Bacterial infections have become a threat to human health because of antibiotic resistance. Carbapenemase enzymes are produced by enterobacteriaceae that are resistant to carbapenem class of antibiotics by disabling the drug molecules. On the list of antibiotic-resistant priority pathogens published by World Health Organization in 2017, bacterial families of critical level are carbapenem resistant. It has been reported that bacteria producing KPC-2 (class A carbapenemase enzymes) have recently been seen in a growing number and resistance.<sup>1</sup>

The purpose of this study is to search for new carbapenemase inhibitors that may be effective against such bacteria. For this goal, binding affinities of the recently synthesized arylcoumarin derivatives<sup>2</sup> for carbapenemase KPC-2 were calculated with molecular docking.

Structures of 39 arylcoumarin compounds were optimized by PM6 method via conformation scan. The crystal structure of KPC-2 enzyme (pdb code: 20V5) was prepared for docking. The AutodockTools program was used to prepare the enzyme and ligand structures while Autodock Vina program was employed for the molecular docking calculations.

The compounds tested showed good affinity to the carbapenemase (KPC-2) enzyme. Binding energies ranged from -7 to -11 kcal/mol). The highest binding affinity belongs to the benzocoumarin derivatives. These compounds are promising candidates as carbapenemase inhibitors.

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## P67-Unusual disproportionative condensation of indoles with cyclohexanone: an experimental and computational study<sup>1</sup>

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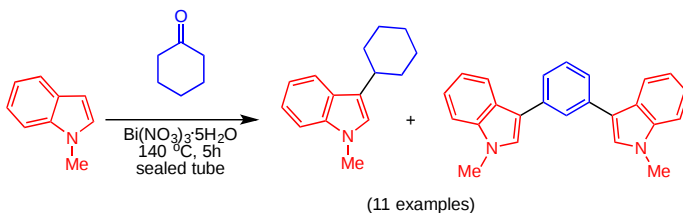
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The indole nucleus represents a privileged heterocyclic scaffold in medicinal chemistry, which is widely found in the structure of biologically active natural and synthetic products.<sup>2</sup> Therefore accessing functionalized indoles has been attracted the attention of both synthetic and medicinal chemists.<sup>3</sup> In this study, the synthesis of C3-cyclohexyl substituted indoles and 1,3-di(1*H*-indol-3-yl)benzene derivatives via the bismuth nitrate-promoted unusual disproportionative condensation of indoles with cyclohexanone are reported for the first time. The plausible formation mechanism for the products is provided and supported with DFT (M06-2X/6-31+G(d,p)) calculations. Structures of the products were elucidated on the basis of 1D, 2D NMR techniques, and HRMS analysis. All computations have been carried out using the Gaussian 09 program



package.<sup>4</sup>

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## P68-A combined experimental and theoretical study for the formation of indolizine, pyrrolo[1,2-a]pyrazine, pyrrolo[1,2-a]pyrazinone

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Indolizines are aromatic systems; having a bridgehead nitrogen atom shared by an electron-excessive and an electron-deficient ring.<sup>1</sup> Indolizines have attracted considerable interest due to their observed pharmaceutical activities such as anti-inflammatory, antitumor, and CNS (central nervous system) activity.<sup>2</sup>

Our objective was to understand the effects of different types of amines in the cyclization of *N*-propargyl carbaldehyde **1** and enlighten the mechanism by means of theoretical calculations (Figure 1). The potential energy surfaces along the reaction pathways were examined by means of DFT (density functional theory) calculations. Calculated activation barriers for the cyclization reactions were investigated in the light of experimental findings.

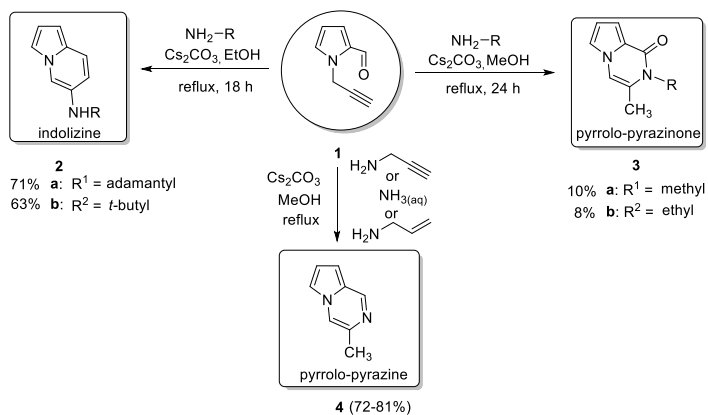


Figure 1

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## P69-Gels confined to narrow capillaries

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Flow of soft matter objects through one-dimensional environments is important in industrial, biological and biomedical systems. Establishing the underlying principles of the behaviour of soft matter in confinement can shed light on many artificial and natural systems. We report an experimental and theoretical study of translocation of  $\mu\text{m}$ -size hydrogels (microgels) through microfluidic channels with a diameter smaller than an unperturbed microgel size (see Fig. 1). For microgels with different dimensions and mechanical properties, under a range of applied pressures, we established the universal principles of microgel entrance and passage through microchannels with different geometries. We also show a non-monotonic change in the flow rate of liquid through the constrained microgel, governed by its progressive confinement. Experimental results were in agreement with the theory for non-linear deformation of gels. Our work has implications for a broad range of phenomena, including occlusion of blood vessels by thrombi and needle-assisted hydrogel injection in tissue engineering.<sup>1</sup>

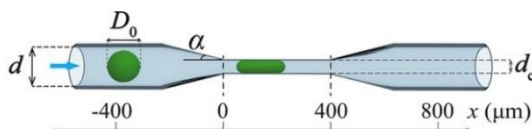


Figure 1: Microgels move along the direction indicated by the arrow, under the pressure drop applied along the microfluidic channel.

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# P70-Intermolecular interactions between protoporphyrine and hydroxypyrene

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In this study, we investigated intermolecular photoinduced donor-acceptor complexes between protoporphyrin (Proto) and 1-hydroxypyrene (PyOH) spectroscopically and computationally. Porphyrins, photoactive materials, have important applications such as molecular electronic devices and photosensitizers in photodynamic therapy of cancer<sup>1</sup>. The conformational analyses of investigated molecules were performed to determine initial structures. Full optimizations were performed with Gaussian 09<sup>2</sup> at the  $\omega$ B97XD/6-31G(d,p) level. In order to explore the solvent effect, solvation calculations were performed by Tomasi's Polarizable Continuum Model (PCM)<sup>3</sup> using tetrahydrofuran (THF) and water as the solvents. Molecular orbitals and energy differences of frontier orbitals and electrostatic potentials for studied molecules calculated at  $\omega$ B97XD and B3LYP/6-311++G(d,p) level in gas phase and in different media. PyOH-Proto complexes are stable in the gas phase and in studied solvents. Fluorescence spectra of PyOH show changes in intensity with addition of increasing amount of protoporphyrin. Figure 1 shows the UV-Vis absorption spectra for Py-Proto for comparison.

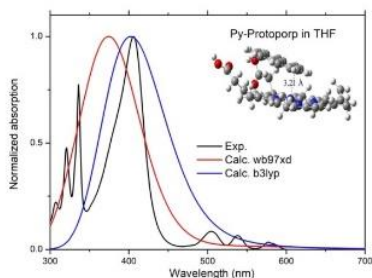


Figure 1. Comparison of calculated and experimental UV-Vis absorption spectra of Py-Proto in THF

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We acknowledge computer time on FenCluster provided by Ege University Faculty of Science

## P71-Singlet oxygen generation aptitude of thiophene-derivatives

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Dithienylpyrrole (DTP)<sup>2</sup> dyes have been recently synthesized and their optical properties have been investigated using TD-DFT with static and dynamic calculations.<sup>2</sup> Two photon absorption<sup>3</sup> values of these organic dyes showed high-cross sections in the infrared region, which underlines their potential use as efficient sensitizers in photodynamic therapy. The present study aims to provide a full characterization of the photophysical properties of DTP's using different photophysical pathways leading to intersystem-crossings, where triplet manifold population will be essential for the subsequent production of singlet oxygen. The linear and non-linear optical properties will be studied taking into account the influence of dynamical and vibrational effect by Wigner distributions<sup>4</sup> and spin-orbit coupling between low-lying singlet and triplet states will be also considered.

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# **P72-A software tool for parallel computation and characterization of residue interaction energies from molecular dynamics simulations**

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Ligand binding to proteins often induce allosteric effects, characterized by signals transduced throughout the structure. The effect of the ligand may result in large-scale backbone rearrangements as well as subtler changes within the structure. In the latter case, mechanistic basis of allostery can only be elucidated by an overall characterization of residue interactions on the side-chain level. Molecular Dynamics simulations have been used in past to identify such subtle allosteric mechanisms by using Protein Energy Networks<sup>1</sup> and/or Interaction Energy Correlation Analysis<sup>2</sup>. Both approaches require the calculation of all possible pairwise residue interaction energies over the course of simulation time. This can be complicated and time-consuming even for small proteins if the interacting residue pairs are not properly selected in a single-threaded computation task. We present here a practical and easy-to-use tool with a terminal and a simple Graphical User Interface for the calculation of residue interaction energy time series from NAMD-generated MD simulation trajectories. The tool features parallel computation of interaction energies and allows custom residue and distance cutoff selections.

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## **P73-Molecular modeling of metal organic frameworks for the controlled release of topical steroids**

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Inflammatory skin diseases such as dermatitis (eczema), seborrheic dermatitis, and psoriasis are the most common problems in dermatology. The most effective and commonly used drugs for treating inflammation are the topical steroids. Topical corticosteroids are typically used for only short periods of time with a dosage control because they exert some negative side effects on skin. The unconscious over dosage of steroids formulated as cream or gel forms causes loss of the healthy tissue and even damages human organs like kidney and liver. Metal-Organic Frameworks (MOFs) are obtained by the self-assembly of metal clusters and organic linkers, resulting in high pore volumes, large surface areas, and tuneable pore size. MOF's are widely used for drug delivery applications.

In this study, the properties of mesoporous MIL-101(Cr) is investigated computationally to examine its performance in control steroid release for the prolonged and better control of drug administration. Various steroids of different potent were studied as the anti-inflammatory drugs. Grand Canonical Monte Carlo (GCMC) and Molecular Dynamics (MD) simulations are done by using Materials Studio 2017. GCMC method was used to calculate the steroid storage capacity of MIL-101(Cr) and isosteric heats at varying steroid loadings. By the help of Simulated Annealing method, interacting atoms of the steroids and the framework are determined at lowest energy configurations of the steroids.

## P74-A Mechanistic study on the catalytic mechanism of protein arginine deiminase 2

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The protein arginine deiminases (PADs) catalyze the post-translational hydrolysis of peptidylarginine to form peptidyl-citrulline in a process termed deimination or citrullination that are calcium-dependent enzymes that use a nucleophilic cysteine to hydrolyze guanidinium groups on arginine residues to form citrulline. This reaction results in the loss of positive charge, thereby affecting protein function and altering protein–protein and protein–nucleic acid interactions. Humans encode five PADs, designated PADs 1–4 and PAD6, which are highly homologous both within and between species. Recent work suggests that PAD2 also plays an important role in both extracellular trap formation and in gene regulation. Kinetic studies revealed that PAD2 distinguished from other members of the family by following a substrate-assisted mechanism during catalysis. Given the current interest in PAD2 as a therapeutic target in breast cancer, the aim of the study is to elucidate the reaction mechanism of PAD2 using a multiscale approach that would combine quantum mechanics, molecular dynamics. The catalytic mechanism using model systems (Figure 1) and high level quantum mechanical calculations at M062X/6-31+G(d,p) level of theory were performed.

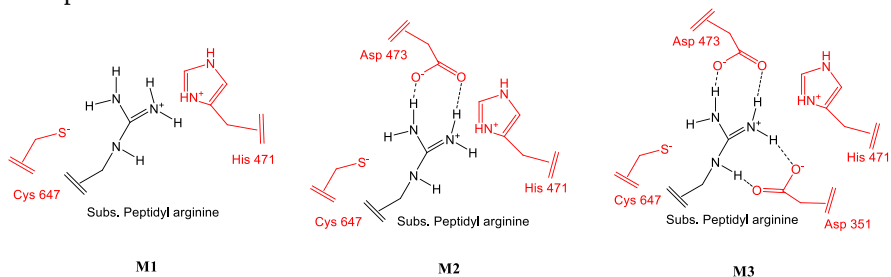


Figure: Defined models for QM studies

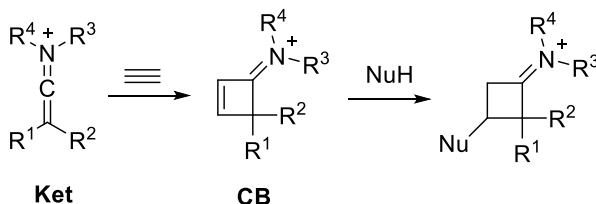
# P75-Michael addition reaction of cyclobuteniminium salts and various nucleophiles - a DFT study

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Cyclobutanones are one of the pivotal building blocks in organic synthesis.<sup>1</sup> However, it is hard to access  $\beta$ -substituted cyclobutanones using vinyl ethers and enamines with Ghosez's procedure since vinyl ethers and enamines do not give rise to cycloaddition reaction.<sup>2</sup> Recently, an efficient general method to access  $\beta$ -substituted cyclobutanones via the one-pot [2+2]/(hetero)-Michael reaction was reported.<sup>3</sup> Functionalized Michael adducts can broaden the use of cyclobuteniminium salts and cyclobutanones in organic synthesis. In this context, Michael reactions of cyclobuteniminium salts with a broad range of nucleophiles were investigated and reactivity differences between nucleophiles were rationalized by DFT (Scheme 1).



**Scheme 1.** Michael reactions with cyclobuteniminium salts (CB)

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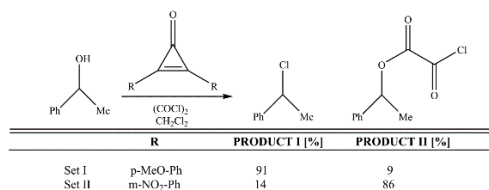
# P76-A computational insight into cyclopropenone activated dehydration reaction of alcohols

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The cyclopropenone activated dehydration reaction of alcohols is a promising alternative to alcohol substitution reactions to avoid hazardous byproducts and harsh reaction conditions. In a recent study, chlorodehydration of alcohols was investigated by Lambert et al. and two possible reaction mechanisms were proposed. The aim of this work is to elucidate the details of the chlorodehydration reaction mechanism in the presence of cyclopropenones. In this regard, a comprehensive density functional theory study was conducted for the proposed reaction mechanisms with the reactants in Set I and Set II (Scheme I). Furthermore, the electronic and steric effects of the substituents on the barriers also investigated by exchanging their p- and m- descriptors. Geometry optimizations and frequency calculations were performed at the M062X/ 6-31+G(d,p) level of theory of the Gaussian 09 software in dichloromethane at room temperature. The results indicated that an alternative path is more probable for the formation of PRODUCT I.



**Scheme 1.** Experimental results of cyclopropenone catalyzed chlorodehydration reaction.

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# P77-ZnO and TiO<sub>2</sub> loaded MnO<sub>2</sub> nanocomposites and photoactivity investigation

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TiO<sub>2</sub> and ZnO are most extensively used in the photocatalytic systems owing to their complementary physicochemical properties and high efficacy. However, poor adsorption capacity, formation of rapid aggregates in suspension and recycling difficulties make the utilization of bare TiO<sub>2</sub> and ZnO difficult. In recent years, strategies have been focused on the usage of adsorbent materials as support for TiO<sub>2</sub> and ZnO particles. Materials with large surface area and porous morphology are used as high efficient adsorbent. Manganese dioxide is one of the most interesting material with different physical and chemical properties, such as crystallinity, amount of combined water, specific surface areas, and electrochemical performance. Its structure and unique chemical properties are taken advantage of in potential applications such as cation-exchange, adsorbents, sensor, battery, catalysis. MnO<sub>2</sub> also possesses good adsorptive ability to remove organic pollutants and heavy metals in wastewater. MnO<sub>2</sub> draw attention for utilizing in the adsorption systems due to the porous structure and eco-friendly nature. Taking into then consideration that, in this study, MnO<sub>2</sub> is used as the support material for TiO<sub>2</sub> and ZnO nanoparticles. The aim of this work is to synthesize MnO<sub>2</sub> supported TiO<sub>2</sub> and ZnO nanocomposites and investigate their adsorptive and photocatalytic performances. The structural features of TiO<sub>2</sub>- and ZnO-loaded MnO<sub>2</sub> nanocomposites were investigated by X-ray diffraction (XRD) and scanning electron microscopy (SEM). XRD analysis supplies information about the crystalline sizes of TiO<sub>2</sub> and ZnO nanoparticles. SEM images reveal obvious variations in the surface morphology of raw MnO<sub>2</sub> after TiO<sub>2</sub> and ZnO loading. For the photocatalytic experiments, methyl orange (MO), which is a water soluble azo dye produced in industrial processes, is selected as the model compound. The photocatalytic activities of the supported catalysts are examined for decolorization processes of MO solutions under UV irradiation.

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## P78-Understanding the impact of thiophene/furan substitution to intrinsic charge-carrier mobility

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One of the major challenges in rationalizing the intrinsic influences of molecular fine-tuning on charge-transport in organic semiconductors is due to changes in molecular packing. Thus it is, to a limited extent, desirable to elaborate materials to exhibit similar packing arrangements but slightly differ in their molecular structures. A molecular system, consisting of a heterocyclic core flanked by phthalimide end-capping units, is promising to overcome this issue.<sup>1</sup> XRD measurement reveals that, when bithiophene (bi-T) core was replaced by bifuran (bi-F), (see Figure 1) the molecular packing was largely maintained while the resulting difference in charge-transport is substantial. Even though their optical and thermal measurements show minimal change, transistor measurements reveal that substituting bi-T with bi-F results in more than one order of magnitude increase in hole mobility (*i.e.*,  $1.7 \times 10^{-3}$  vs.  $2.6 \times 10^{-2}$  cm<sup>2</sup>/Vs) but, quite surprisingly, an unusual loss in electron mobility (*i.e.*, 0.21 vs. 0.0 cm<sup>2</sup>/Vs). In this study, we aim to theoretically understand the influence of heteroatom substitution on structure-property relationship in bi-F and bi-T via utilization of multi-scale computational procedure. Various electronic, optical and geometrical properties of the derivatives are calculated by the means of Density Functional Theory (DFT) and Time-dependent DFT (TD-DFT) at B3LYP/6-311G\*\* level of the theory. Quantum mechanical calculations are accompanied by Molecular Dynamics and MOO/ZINDO calculations.

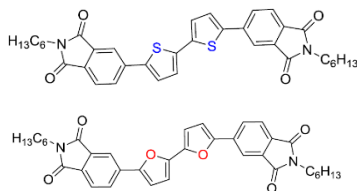


Figure 1. Structures of bi-T (top) and bi-F (bottom)

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## **P79-Photocatalytic decolorization of reactive Blue 221 on TiO<sub>2</sub>: prediction of mechanism via conceptual DFT**

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Reactive dyes are anionic dyes that are extensively used in textile industry and they constitute 12% of the worldwide production of the commercialized synthetic dyes. Discharging of these reactive dye effluents into water streams after the dyeing and finishing processes in the textile industry can cause severe environmental problems. Conventional treatment methods are either ineffective to remove them from wastewater or they only transfer them to another phase causing a secondary pollution. TiO<sub>2</sub> photocatalysis is an alternative approach for decolorization of azo dyes in waste water. This technique is based on the generation of highly reactive hydroxyl radicals and photogenerated valence holes when TiO<sub>2</sub> particles are irradiated by UV light. The aim of this study is to develop a shortcut method to predict the intermediates and the mechanism of decolorization reactions of azo dyes. To this purpose, Reactive Blue 221 (RB221) was chosen as the representative member of azo dyes and photocatalytic decolorization reaction of RB221 in the presence of TiO<sub>2</sub> under UV-A light irradiation was investigated. TiO<sub>2</sub> was synthesized by a modified sol-gel method from an alkoxide precursor and characterized by XRD, XPS, ESEM-EDX and BET measurements. The decolorization reaction was monitored by UV-vis, FTIR, GC-MS and ESEM-EDX techniques. Conceptual Density Functional Theory was applied to the degradation reaction of the target molecule and reactivity descriptors were calculated by means of DFT/B3LYP/6-31G\* level of theory. Eventually, the reactive sites of the molecule for •OH radical attack were determined and the reaction mechanism was predicted by combining the results of the DFT calculations with the experimental FT-IR and GC-MS analyses. The results of the study suggest that TiO<sub>2</sub>/UV photocatalysis may be used as a method for treatment of diluted wastewaters in textile industries, adsorption on TiO<sub>2</sub> surface occurs through sulfo and carbonyl groups of the dye molecule, while decolorization by the breaking of the azo bond.

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## 80-The binuclear CuAAC mechanism in the light of new experiments

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CuAAC, Copper Catalyzed Azide Alkyne Cycloaddition Reaction, has been utilized in thousands of synthetic pathways since its first report, but the debate on the mechanism has continued for a long time. In first studies, the starting copper acetylide structure was suggested as a mononuclear species however, kinetic studies have shown later that the reaction is 2<sup>nd</sup> order with respect to copper. Many theoretical and experimental studies have supported the multinuclear nature of the reaction. In a recent experimental study, isotopic Cu labelling experiments were carried out to elucidate the number of copper atoms involved in the reaction [1]. The obtained product could only be explained by a ligand exchange mechanism between the two Cu(I) centers in a dinuclear intermediate. In this study, we aimed to elucidate the reaction mechanism by mimicking the experimentally carried reaction. Possible ligand exchange steps in the previously proposed mechanism have been modelled by DFT calculations in the presence of N-heterocyclic ligands (NHC). This study has fulfilled its ultimate aim by explaining the ligand exchange and the experimentally observed isotopic enrichment with specific attention to the number of copper atoms that participate in the reaction. The calculations were performed with M06L functional with the 6-31+g(d,p) basis set in tetrahydrofuran and for Cu, LANL2TZ effective core potential was used.

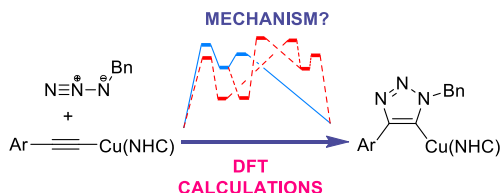


Figure 1. The CuAAC Reaction<sup>2</sup>

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## **P81-the inhibitory effect of quinone derivatives on oacetylpeptidoglucan esterase enzyme**

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O-Acetylpeptidoglycan esterase (APE1) enzyme is a member of SGNH hydrolase family and it controls the growth and division of bacterial cell wall. In this respect, it is a potential target for studies on antibiotics and their resistance to some bacteria. In this study, lead molecules that show inhibitory effects were investigated and a set of nine active inhibitors of Ape1 were selected. For this purpose, Molecular dynamics simulations were performed with Amber 16 and different frames of the receptor were obtained. Docking analysis were done on these receptor structures and binding scores were calculated. Comparison of the scores have shown that the results are compatible with the experimental  $K_i$  values of the test molecules. A virtual screening was performed based on quinone structures that have shown inhibitory effect in a recent study.<sup>1</sup> 20.448 molecules were obtained to dock into the APE1 enzyme. The calculations have shown that various molecules can be found that show inhibitory action on APE1 enzyme and thus serve as a potential target for development of antibiotics.

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## **P82-Dynamical origin of room-temperature charge-transport in organic crystal**

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We present a critical assessment of the two fundamental dynamical models used to describe charge transport in organic semiconductor materials, namely the delocalized band model and the localized hopping model. We aim to determine the extent to which each of these models provides a reliable, and possibly quantitative, prediction of experimental charge mobilities in a variety of OSMs in conditions typical of practical applications, and to provide a conceptually simple and general approach to combining the two models to extend their range of applicability.<sup>1</sup>

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## P83-Investigation of allosteric pathways on the bacterial ribosome

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Allosteric communication pathways from the decoding center to the sarcin-ricin loop (DC-SRL) and the peptidyl transferase center (DC- PTC) were investigated for the bacterial ribosome 70S using computational approaches. For this aim, the x-ray structure (4kdk-4kdj) and 100 atomistic conformers generated with the ClustENM method were used [1]. Twenty shortest pathways were calculated for each conformer using elastic network model-type interactions [2] and Yen's Algorithm [3]. On the allosteric pathways between DC-SRL, EF-G stands out with critical sites on its domains IV and V, which correspond to quite conserved regions. Domain IV has a significant function in blocking back translocation of tRNA. On the DC-PTC pathways, G2553 and U2506 stand out as important conserved residues, where the latter appears as a drug binding site [4].

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## **P84-Investigating self-assembly behaviour of lipid-like structures in dual solvents**

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Dissipative particle dynamics (DPD) is a coarse-grained simulation method. It is particularly useful for investigating properties of self-assembled molecular systems at the mesoscopic level, including biopolymers such as lipids and peptides<sup>1-3</sup>. In this work, we explore parameters influencing the phase behavior of linear (lipid-like) and symmetrically branched (lipidoid-like) block copolymers in a binary solvent via DPD for different compositions and concentrations. Our coarse-grained models consist of four types of beads: covalently bound copolymer beads, A and B, and solvent beads, C and D. Specifically, A and B are mildly repulsive towards C and D, respectively, while C and D are strongly repulsive towards each other, as are A and B. Equilibrium morphologies obtained via DPD demonstrate formation of miscellaneous structures including hollow spherical and hollow cylindrical micelles which may be altered by changing the composition and concentrations of the block copolymers. Interesting phase behavior for the lipidoid-like structures in the dual solvent is observed, whereby instead of the usual spherical to cylindrical phase transition that is observed as the concentration is increased, cylindrical/spherical mixed phases appear at intermediate values while interacting spheres of various sizes are recovered at higher density. Structures of the micelles are characterized by radial distribution functions and form factors. The latter are useful in determining size distributions of the morphologies. This work provides insight into the self-assembly of lipid-like structures. The rules of thumb obtained are expected to guide designed structures for polymer-based drug delivery applications and nano-reactor synthesis.

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# **P85-Molecular modelling and docking studies on 3-oxoacyl-[acyl-carrier-protein] reductase enzyme (FabG) of *Toxoplasma gondii***

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The 3-oxoacyl-[acyl-carrier-protein] reductase enzyme (FabG) (EC:1.1.1.100) is a part of the type II fatty acid synthesis system (FASII) which is responsible for the elongation and formation of the fatty acid long chain. FabG catalyses the  $\beta$ -ketoacyl-ACP reduction to  $\beta$ -hydroxyacyl-ACP products by NADPH – dependent manner. Enzymes of the fatty acid synthesis system of the Apicomplexan parasites which cause severe diseases including malaria and toxoplasmosis are considered as druggable targets due to FASII system which is essential for the apicoplast maintenance and biogenesis and also pathogenesis<sup>1,2,3</sup>. In this work, we have conducted a computational study to understand structural features of the *Toxoplasma gondii* FabG enzyme including a molecular docking approach with coumarin derivatives to identify potential inhibitors. Basic Homology Modelling was conducted by both Modeller9.15 program and the Swiss-Modeller server via a Plasmodium Falciparum FabG template (PDB ID: 2C07) with 56% identical alignment at 64% query coverage in Basic Local Alignment Search Tool (BLAST). These two models were taken to Chimera 1.11.2 for structure minimisation. The total of four models (two minimised and two untampered) were thereafter assessed by various structure validation servers. Schrödinger's Glide was used for the molecular docking analyses. In the first step, the best 20 coumarin derivatives among 38 were selected by SP docking and then XP module was used to select the most potent ones. DeltaG binding free energy was predicted by MM-GBSA method for each poses. According to the molecular docking results; while XP Gscores were between 11.450 and 6.989 (-kcal/mol), MM-GBSA DeltaG was found to be 53.870 and 56.083 (-kcal/mol) for the most potent ones. As a result of this *in silico* study, 7 coumarin derivatives were selected for further *in vitro* enzyme inhibition studies. FabG enzyme located in the type II fatty acid synthesis system is a promised drug target for the treatment of toxoplasmosis and due to

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structural homology any inhibitor found for the TgFabG would be also used for the treatment for the other Apicomplexan parasites.

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