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Crystal Structure of Two Biologically Active Biphenyl Derivatives. Nancy Naguib[a], Ibrahim Farag [b], Zein K. Heiba[a], Karimat El-Sayed[a]. [a]*Physics Department, Faculty of Science, Ain Shams University, Cairo, Egypt*. [b]*National Research Center, Cairo, Egypt.*
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The structure of two biphenyl derivatives was investigated by X- ray single crystal diffraction technique. The first compound is 6-(2-biphenyl-4-ylethyl)-4,5-dihydropyridazin -3(2H)-one, $C_{18}H_{18}N_2O$, with molecular weight: 278.355 , monoclinic, $P2_1/c$, a=7.2564 (3)Å, b=8.8986 (3)Å, c=23.2598 (11)Å, β = 100.00(18)°,V = 1471.00(11)Å^3, Z = 4,Dcal = 1.523Mgm^{-3}, μ = 0.08 mm^{-1}, with 1022 observed reflections (R (int) = 0.032), λ (MoK_α) = 0.71073Å, final R and wR are 0.044 and 0.081, respectively. While the other compound is (5Z)-6-biphenyl-4-yl-4-oxohex-5-enoic acid, $C_{18}H_{16}O_3$,with molecular weight: 280.323, monoclinic, $P2_1/c$, a=15.2407 (13)Å, b=7.9037 (6)Å, c=12.9131 (8)Å, β = 110.116 (3)°, V = 1460.6 (2)Å^3, Z = 4,Dcal = 1.275Mgm^{-3}, μ = 0.09 mm-1, with 882 observed reflections (R(int) = 0.049), λ (MoK_α) = 0.71073Å, final R1 and wR2 are 0.058 and 0.115, respectively. There are four crystallographically independent molecules in the asymmetric unit of the two compounds. The molecules are stabilized by C-H…N, C-H…O and C-H…N types of intermolecular hydrogen bonds in the unit cell in addition to van der Waals forces.

Key words: **crystal structure; conformation; COX**

FA1-MS07-P14

Molecular and Crystalline Structure of Two New Nitrogen-Sulphur Pro-Ligands from Single Crystal Diffraction Data and Solid-State DFTB Calculations. Edward E. Ávila[a], Asiloé J. Mora[a], Gerzon E. Delgado[a], Ricardo R. Contreras[a], William Mendéz[a], Alexander Briceño[b]. [a]*Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida, Venezuela.* [b]*Instituto Venezolano de Investigaciones Científicas, Centro de Química, Altos de Pipe, Venezuela.*
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The complexity of problems dealt by bioinorganic chemistry begins with the development of model compounds of low molecular weight. These models mimic the properties of active metal sites in metabiomolecules of interest, which allow the understanding of the role played by metal ions in biological processes. In particular, efforts [1] have been made to reproduce the pseudo-tetrahedrical coordination spheres of metal ions linked with pro-ligands containing two nitrogen atoms and two sulphur atoms as donor groups, since Nature has used this type of surroundings in the coordination of metal ions such as, for example, Cu(II) in plastocyanin or azurin [2]. Contreras *et al*., [3-4] have recently designed and synthesized a series of bidentated nitrogen-sulfur pro-ligands shown in Fig. 1. These compounds have been made available as single crystals.

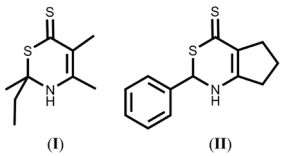

Figure 1

Diffraction data for the compounds: 2-ethyl-2,4,5-trimethyl-2H-1,3-thiazine-6(3H)-thione (**I**) and 2-phenyl-1,2,6,7-tetra hydrocyclopenta[d][1,3]thiazine-4(5H)-thione (**II**) were collected on a Rigaku AFC7S diffractometer using the programs *CrystalClear* [5] for the data collection and cell refinement, *CrystalStructure* [6] for the data reduction, and *SHELX97* [7] for the structure solution and refinement. The solution of their crystal structures found 1 fragment (12 non-hydrogen atoms) for compound (**I**) and 2 fragments (32 non-hydrogen atoms) for compound (**II**). The molecular packings consist of zig-zag chains with hydrogen bonds of the type N-H···S with gaph symbols $[C(6)]_S$ for (**I**), $[C^2_2(12)]_{S1}$ and $[C^2_2(12)]_{S3}$ for (**II**). Finally, the molecular structures obtained by X-ray single diffraction are compared with the ones optimized by solid state DFTB calculations [8].

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Keywords: bioinorganic compounds; solid-state DFTB calculations

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A Thermodynamic Comparison of Hydrophobic vs. Hydrophilic Ligand-Protein Interactions. Caitriona Dennis[a], Neil Syme[a], Agnieszka Bronowska[a], Steve Homans[a]. [a]*Institute of Molecular and Cellular Biology, University of Leeds, Leeds LS2 9JT, U.K.*
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Highly specific molecular recognition is the driving force behind every biological process. Carefully tuned affinities govern the intricate recognition event but despite the universal nature of these interactions, our understanding of their molecular basis is limited. This limited knowledge, in turn, compromises the structure-based drug design of small molecules that modulate these interactions. The limited ability to predict ligand affinity is largely due to the complexity of all the contributions from the ligand, the protein and solvent rearrangement. In order to gain a better understanding of ligand binding, the global thermodynamics of ligand binding within two classical systems has been

examined. Using two proteins from the lipocalin family, the binding signatures of a model hydrophobic system (MUP – Mouse Urinary Protein) has been compared with that of a model hydrophilic system (HBP – Histamine Binding Protein). A combination of techniques including X-Ray crystallography, NMR, Isothermal Titration calorimetry and Molecular Dynamics has been able to show that both systems bind ligands with a similar overall entropy of binding yet the contributions arising from protein, ligand and solvent are very different.

Keywords: thermodynamics; ligand-binding; lipocalin

FA1-MS07-P16

Structure Determination of 2 Potential Parasitic Drug Targets of the SAHH Family. Marina Siponen[a], Magdalena Wisniewska[a], Tobias Karlberg[a], Ann-Gerd Thorsell[a], Johan Weigelt[a], Herwig Shüler[a]. [a]*Structural Genomics Consortium, Karolinska Institute, Stockholm, Sweden.*
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S-adenosyl-L-homocysteine (AdoHcy) is a product but also a potent feedback inhibitor of several methyltransferases which use S-adenosyl-L-methionine (AdoMet) as a methyl donor. The S-adenosyl-L-homocysteine hydrolases (SAHHs) catalyse the reversible reaction of AdoHcy to adenosine and homocysteine [1]. Consequently, SAHHs play a critical role in maintaining a normal level of AdoHcy in the cell. Inhibition of SAHH results in cellular accumulation of AdoHcy, inhibiting AdoMet-dependant methyltransferases. Since methylation plays a role in a wide range of cellular processes, the inhibition of SAHH has been proposed as a drug target for several parasitic diseases including malaria and leishmaniasis [2, 3]. We report here the crystal structures of 2 SAHHs from the human parasites *Leishmania major* and *Trypanosoma brucei*. The structure of the human SAHH being determined (PDB ID = 1LI4), our results can provide an initial structural perspective towards the development of anti-parasitic strategies.

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Keywords: parasites; nucleoide metabolism; protein structures

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DNA Flipping by Restriction Endonucleases. Roman H. Szczepanowski[a,b], Honorata Czapinska[a,b], Michael Carpenter[c], Mindaugas Zaremba[d], Gintautas Tamulaitis[d], Virginijus Siksnys[d], Ashok Bhagwat[c], Matthias Bochtler[a,b,e]. [a]*IIMCB, Trojdena 4, 02-109 Warsaw, Poland.* [b]*MPI- CBG, Pfotenhauerstr, 108, 01309 Dresden, Germany.* [c]*Department of Chemistry, Wayne State University, Detroit MI 48202, USA.* [d]*Institute of Biotechnology, Graiciuno 8, LT-02241, Vilnius, Lithuania.* [e]*Schools of Chemistry and Biosciences, Main Building, Park Place, Cardiff University, Cardiff CF10 3AT, UK.*
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Nucleotide flipping, the extrusion of a base from the base stack in the helix into an extrahelical position, is a well-known process, that can occur spontaneously, but is rare. Many enzymes promote this drastic distortion of DNA, usually because they need access to the base to excise it or to alter it chemically. In some cases, the flipping also provides access to a damaged estranged base in the stack. We have discovered the first instance of nucleotide flipping in restriction endonucleases. Flipping in this group of enzymes is unusual for several reasons: (a) It naturally occurs with intact base pairs, and is not intended to detect or repair a lesion. (b) Nucleotides in both DNA strands are flipped, and the DNA is compressed. The other enzyme classes usually flip only one base and leave the estranged base in place to prevent DNA compression. (c) In some cases (Ecl18kI), flipping serves to "skip" a base pair in a pseudopalindromic target sequence [1]. (d) In other cases (PspGI, EcoRII), it helps to distinguish A:T pairs from G:C pairs with a million-fold specificity [2,3]. Our structures of Ecl18kI and PspGI highlight this previously "unrecognized" use of nucleotide flipping.

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Keywords: nucleotide flipping; pseudopalindromic sequence recognition; protein-nucleic acid complex