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SYNTHESIS PAPER

entitled

QUANTIFICATION OF THE CHEMICAL BOND WITHIN ORTHOGONAL SPACES OF REACTIVITY. APPLICATIONS ON MOLECULES OF BIO-, ECO- AND PHARMACO-LOGICAL INTEREST

*including the work done and the results obtained in relation to the objectives
 achieved during the research grant*

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on year 2012.

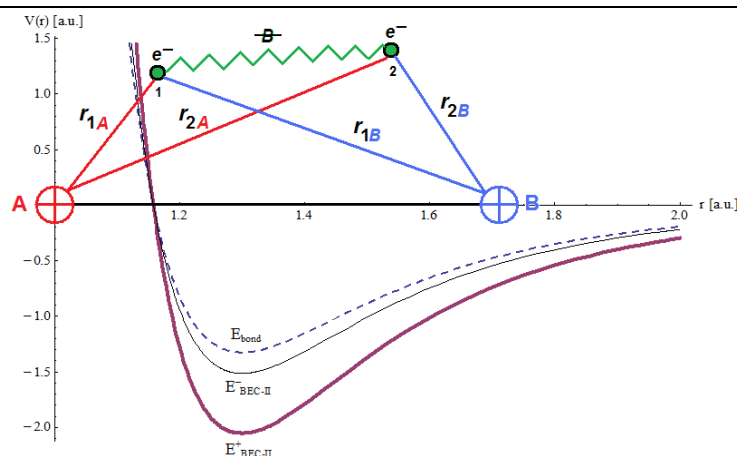
Abstract: The 2012 stage of the present grant had marked the increasingly important conjunction of the topological principles of the atomic and molecular structures with those of the chemical reactivity and biological activity. Thus, by elaborating the multidimensional orthogonal models for the chemical bond of biochemical systems with a carcinogenic impact, of elucidation of the molecular mechanisms of the ecotoxicological systems on atomic and nanostructural basis, as also for the correlation of the chemical reactivity with the bio-eco-pharmacological activity on quantum bases, nanoinformatics and spectral, this stage of research significantly contributes to the formulation of an unitary fermionic-bosonic view and of the quantum information wave-particle for the chemical bond modeling (explanation and prediction of) and of their interactions in extended (nano and mesosystems) molecular structures.

Objectives and Results

1. Elaboration of multidimensional orthogonal models of the chemical and biochemical system with a carcinogenic impact (papers [1- 9]).

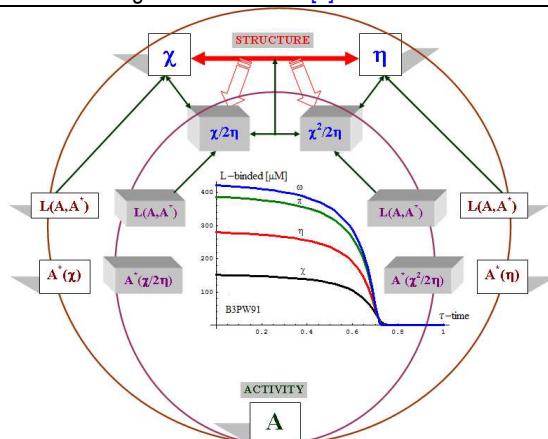
The unification of the bosonic and fermionic theories of the matter is performed to a conceptual level through the Density Functional Theory (DFT), with the aid of the Hohenberg-Kohn extended equations and of functionals of energy corrected with the order parameter, specific of the Bose-Einstein Condensation (BEC). In particular, by the general analytical formulation of the exchange functionals and of correlation, with the aid of the Bogoliubov transformations so that the parameter of condensation order/bosonic seems natural, the formulation of the DFT context where the Gross-Pitaevsky equation specific for the BEC automatically appears was successfully developed. The non-linear character was obtained as a generalization of the Schrödinger equation and allows the connection of DFT with BEC through the Thomas-Fermi approximation; it was further used for the generalization of the classical model Heitler-London of the chemical bond, here for the homopolar bond, but consistent enough to be considered a premise also for the approach of the cyclic systems, aromatic and conjugated systems. This treatment was centered on the new quantum particle responsible for the chemical bond – the *boson bondon* – having as consequence its condensation in the chemical bond, thus explaining the orbitalic paradigm of the bonding-antibonding levels with new BEC specific levels, not yet explicitly explored in an experimental way (Figure 1). The model is conceptually verified by the prediction of interdiction of the He-He chemical bond, even through the bondonic particle, specifying instead new bonding states for the molecule of H₂ susceptible to be experimentally detected in condition of BEC (temperatures of nanoKelvin degree).

Figure 1. Illustration of the bi-atomic chemical bond through the bondonic-bosonic contribution at inter-electronic interaction; the model is overlapped with the states of the molecular hydrogen thus treated, with the highlighting of the BEC levels of bonding (thick line) and antibonding (thin line), both placed under the level of „normal” bonding of the molecule in gaseous state [1].



The hydrogen bond is very important for the chemical-biological interactions, both for the ADN level as for the bonding of the toxicants with the receiver biomolecules from organisms. Thus, the logistic model of kinetics of bonding ligand (chemical)-receiver (biological) is promoted as an innovator mechanism for the hierarchy of the correlations of type chemical structure-biological activity (QSAR) based on the fundamental principles of reactivity, in particular those of electronegativity, chemical hardness, chemical power, electrophilicity, in the same way calculated in various computational frameworks of DFT type for the molecules envisaged for the toxicological analyze *in silico* (Figure 2). The model is illustrated for the chlorinated polycyclic aromatic hydrocarbons (Cl-PAHs) for the biological interaction with the cancerous cells MCG-7 of the human breast, as well for the *Pimephales promelas* and *Rattus Norvegicus* species; the conceptual-computational rules derived from the hierarchy of the correlations based on the computational context and of the one of chemical reactivity generates the so-called BioAct-ChemReact mechanisms of the chemical- toxico/eco/bio/pharmacological interactions, very useful for the prediction of the chemical hazard and of environment for similar interactions or in the same class of chemical compounds or/and biological species.

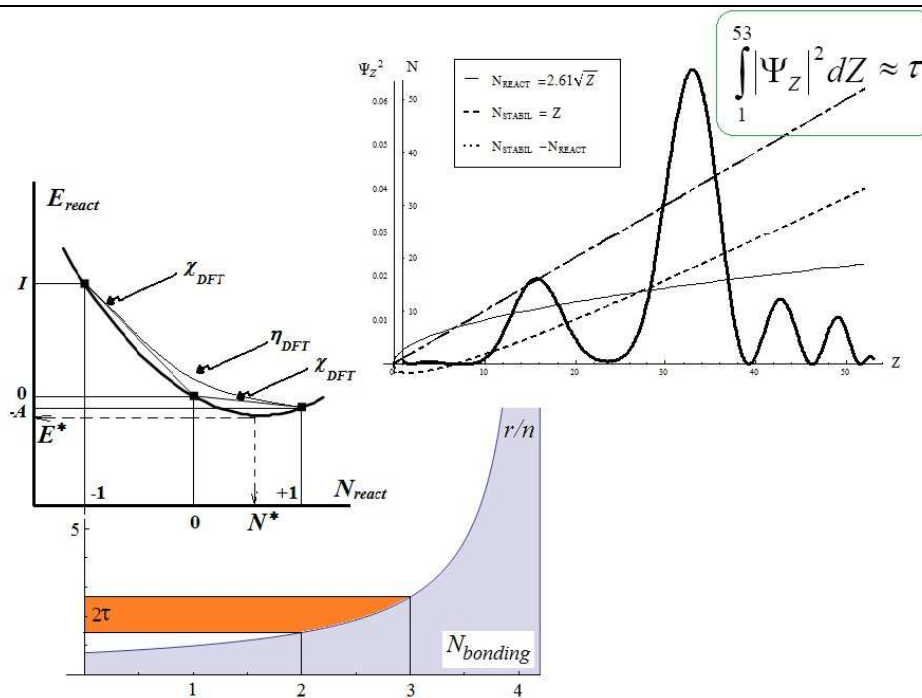
Figure 2. The algorithm of the correlation chemical structure-biological activity through the computational density functional theory (the calculation of the energies E for the highest occupied molecular orbital HOMO and the lowest LUMO) and conceptual through the use of HOMO and LUMO for the electronegativity calculation $\chi = -0.5(E_{HOMO} + E_{LUMO})$, chemical hardness $\eta = 0.5(E_{LUMO} - E_{HOMO})$, chemical power ($\chi/2\eta$) and electrophilicity ($\chi^2/2\eta$); the correlations obtained with the observed activities (A) generate the QSAR models with predicted activities (A*) which together adjust through the feed back the curves of temporal progression of the ligand (L), by those intra-species hierarchy (with different computational bases) and inter-species (with the same computational context) predict the model of the mechanism of chemical reactivity/toxicity involves in the interaction with the bio or eco-logical environment [2].



2. Development of multidimensional orthogonal models of molecular mechanism of ecotoxicologic systems on anatomic and nanostructural bases (papers [10-14]).

In the semi-deterministic context of the electronic density based on the square wave function, of the density functional theory, the quantum mechanical description of the matter is considered in the Bohmian version, in order to be conjugated with the so-called Heisenberg imbalance ($\Delta O \times O = n_o h$) generating a new paradigm of the chemical reactivity, in general, and of the valence state in particular, occasion with which is also clarify the conceptual-analytical difference between the fundamental state and the reactive one (with critical electric charge) in chemical systems (atoms and molecules). Thus, is solved the paradox of the treatment of chemical reactivity from the DFT with a cubical energetic equation, the correct parabolic one being recovered through the so-called double variational mechanism, applied to the Bohmian approach with the quantum potential combined with the golden ratio between the atomic number and the one of electrons, $0.618 = \tau = Z / N$, generalizing the physical state, the non-reactive and the mono-variational ($1 = Z / N$) for the multielectronic systems. The consequences are fundamental, especially for the explanation of the fractional contribution of the electrons in chemical bonding, the natural limitation of the order of chemical bond, for the formulation of some „universal” reference values for electronegativity and chemical hardness, as like for the formulation of a so-called „waves of atomic charge” calibrated at atomic level and with the modeling perspective of the interactions of atoms-in-molecules (Figure 3).

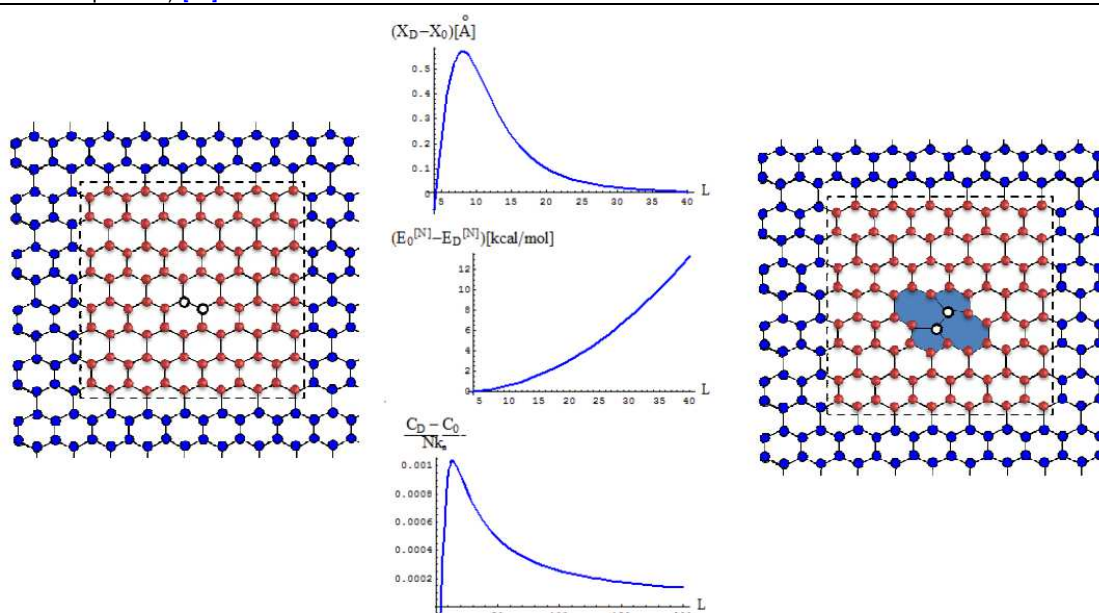
Figure 3. Left medallion: the curve of reactive energy through the parametric dependence of the total energy of electronegativity (χ) and the chemical hardness (η) in density functional theory (DFT in figure) vs. the number of electrons involved in reactivity (N_{react}), together with the curve of the dependence of the length of covalent bond (directly correlated with the atomic ray in the valence state) of the order of bond (directly correlated with the number of electrons in chemical bond); right medallion: the wave function of the atomic charge, overlapped to the reactive and non-reactive dependences of the number of valence electrons (critical) during the first periods of the periodic table of elements, based on the application of the double-variational algorithm involving the Bohmian description of the reactive energetic states with the quantum potential and with the golden ratio ($\tau = Z / N$) [10].



The Bohmian approach of the quantum description of the matter allows the quantification of the chemical bond by the quasi-particle bondon, able to explain through the mass, the energy and the proper length of action the chemical bonding of the extended systems (for graphenes, in area 15 -30 Å), of the nanostructures and of their phase transformations (Figure 4). The applications on graphenes give a valuable premise for the further projections of the design of reactive supports for the pharmaceutical and cosmetic compounds, due to the conductor properties, magnetic and of flexibility

and chemical saturation – unique for these new types of materials (as recognized also by the Nobel Prize in Physics in 2010). Other utilities and promising research directions, based on the bondonic model of nanostructures contain: the description of the optical and acoustic branches through the bondon-phonon interaction, the description of the transitions of phase by the bondonic propagators of 4th order (equal to the maximum of the order of bond in chemical systems), the study of the transitions of phase on defective bases (of order-disorder type), the modeling of nanostructures of „honeycomb” type through the chemical field associated and the specific gauge transformations, the remote quantification of Coulomb`s action, the bondonic identification in the IR and Raman spectra of the chemical compounds, as a size of their reactivity – base of the activity and toxicity bio-, eco- and pharmaco-logical.

Figure 4. The 2D representation of a super-cell of graphene obtained by the extension of the aromatic chemical bonds, in genuine version (ideal, “0”) on the left, and the one topologically modified (“D”) by the Stone-Wales transformations (SW) of the (rotations) type 5/7/7/5; in the middle are represented the variation in the difference of the range, of network energy, and of heat capacity, calculated based on the statistic bondonic informations evaluated between the two nanostructural extremes (without and with topological transformation SW) in relation with the length of the nanosystemic bond (relevant to about 6 consecutive supercells) [11].

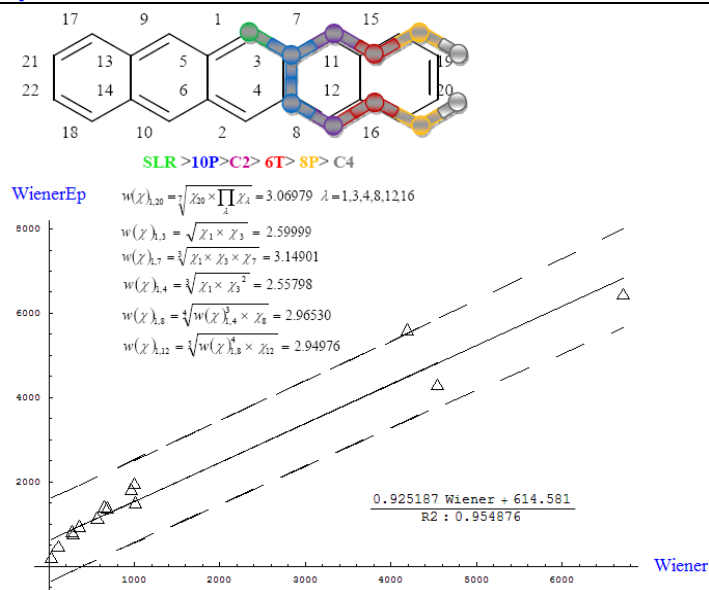


3. Development of new multidimensional orthogonal models for the chemical reactivity correlated to the bio-eco-pharmacological activity by quantum, nanoinformatics and spectral basis (papers [15-21]).

The recognized performances of the molecular topology for the extended chemical systems continue to be increased by considering its „coloring” with the indices of reactivity, of electronegativity type and chemical hardness, calculated with the spectral resolution and ordered based to the external correlation with structural properties as like the energy of formation, Hueckel, ecc.. The coloring itself are accomplished through an original method, development during the present grant, and is based on the so-called „Timisoara-Parma” rules: considering the central symmetry of the molecule or basic supercell of the envisaged extended system, followed by the distribution of the successive values for a given index, for the calculated spectral series, as moving away from the central symmetry, but invariant for the atoms/nodes belonging to each line of symmetry; thus a topological matrix of the nodes is created colored with the chemical reactivity; the matrix of the (chemical) bonds is made considering the geometric averages with the root equal to the number of nodes taken into account on the chemical bond path that adjacent connects the considered nodes (Figure 5); thus result the topological indices (in this case of Wiener type) reagents of electronegativity and chemical hardness, in turn combined in a parabolic topo-reactive energy, that can be further considered in predictions of correlation structure-activity on series with bio-eco and pharmacological impact. Current application on polycyclic aromatic hydrocarbons with toxicological impact confirmed the usefulness of the model and

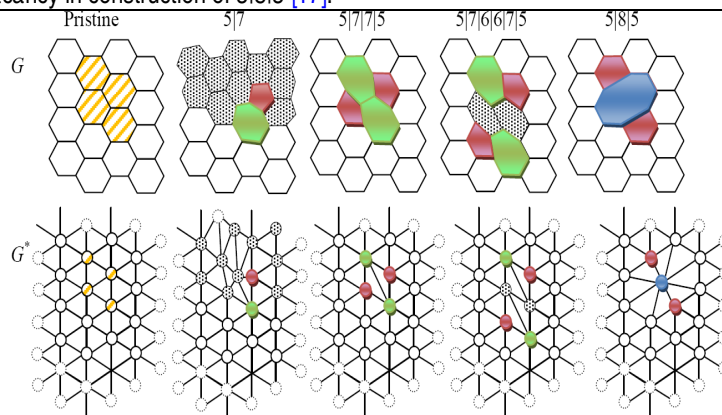
further will be extended and unified with the bondonic approach on researches for any chemical bond with electronic delocalization.

Figure 5. Up: exemplification of topo-reactive coloring for the molecule of pentacene, with the illustration of the way of calculation of the bond between various nodes of the graph associated based on the geometric average of the electronegativity of intermediary nodes, with the root equal with their number; Down: illustration of statistical performances in the correlation of the parabolic topo-reactive energy based on the topo-indices of electronegativity and chemical hardness, in relation with the original Wiener index, for a relevant series of polycyclic aromatic hydrocarbons with bio, eco and pharmacological impact [15].



For the nanosystems support to the biologically active molecules and in particular in pharmaceutical industry, the modeling and the design of the non-defective isomeric networks represents the first interest of the current chemical applied researches. At a fundamental level, for the involved chemical bond, the development of the mechanism of generating of those isomers only by rotations with quasi-crystalline symmetry led to the formalism of the topological generations of type 5|8|5, complementary to those of type Stone-Wales classical (5/7/7/5) of the previous section (Figure 6). First results are promising and refer to the 2D systems of graphenes, for which further can be applied bondonic models of characterization and prediction of the length of action of the chemical binding, as above exposed (Objective 2).

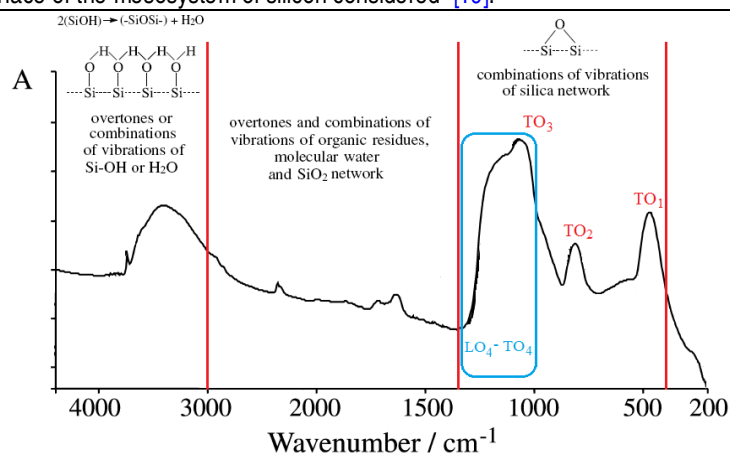
Figure 6. View of direct structure (up) and dual (down) for the graphenic fragments subject to various topological transformations toward the genuine structure ("pristine" in figure): Stone-Wales rotations 5|7|7|5, dipolar dislocations 5|7|6|6|7|5, until the divacancy in construction of 5|8|5 [17].



However, for the mesosystems support to the biological active molecules was advanced an original criterion for ordering and characterizing their porosity, the so-called „spectral inverse quantum „ method (spectral-IQ)”; this is based on the processing of the information from the FTIR molecular

spectra in conjunction with the ratio particle/quantum wave, as abstracted from the recent formalism of Heisenberg extended uncertainty and use the spectral data as the wavelength/wave number for the maximum height for a given band, the limits of considered band, the bandwidth at the halfway of the maximum height (FWHM). The algorithm offers the classification of the mesoporous systems, as those obtained through the sol-gel method, here applied for the N-dodecyl trimethyl ammonium bromide (DTAB) and the cetyl trimethyl ammonium bromide (CTAB) and their combinations as cosolvents, in predominantly porous materials (with accented character of quantum particle, by the tight binding, ionic) and in smooth material (predominantly undulatory of the manifested chemical bond, of covalent type). The results are interpreted by the new index of "residual quantum information", while their validation is made by comparison with the data available from physicochemical analysis, in this case by the thermal decomposition technique at medium and higher temperatures, 60°C and 700°C, respectively. This way, one can identify and reveal new mechanisms of quantum-chemical bonding with spectral correspondent (Figure 7).

Figure 7. General representation of the FTIR spectrum for a mesosystem obtained through the sol-gel method; are noted the transversal optical modes (TO in figure) with the specification of those of rocking TO1, of symmetrical vibration TO2 and anti-symmetrical TO3 of the atoms of oxygen in Si-O-Si bond (being implicit the longitudinal modes LO); the mode LO4-TO4 appears to be a distinct one and undefined assigned in literature, but supposed due to the vibrations induced by the structural disorder from the border of the silicon structure, thus noting as the ideal „territory” for the quantum study (by extracting the inverse quantum information particle/wave of the associated spectrum) of the degree of porosity and of the chemical bond at the surface of the mesosystem of silicon considered [19].



Conclusion and Perspectives

The 2012 stage of this project accomplishes the advancement of an unitary „bundle” of models and algorithms for understanding and controlling the chemical bond in interactions with bio-/eco-/pharmacological environment, i.e.: substantiation of chemical bond on quantum bases of Bose-Einstein condensation with applications to the saturated systems of hydrogen; the extension of the correlations chemical structure-biological activity for the mechanisms of interaction applied with the principles of reactivity (of electronegativity, chemical hardness, chemical power, electrophilicity) with applications to the toxicity inter-species of the chlorinated polycyclic aromatic hydrocarbons; the atomic foundation of chemical reactivity based on the Bohmian quantum potential and on the golden ratio of the atomic number relative to the number of atomic electrons (and of valence); clarification of the relation between the fundamental state and the valence one in the chemical reactive atom, with application on the chemical elements ecotoxicologically active; the extension of the mechanism of formation and bondonic propagation in extended molecular systems, as nanosystems and graphenes; introduction of the concept of reactive-topological coloring through the indicators of electronegativity and the chemical hardness with spectral resolution, with application at polycyclic aromatic toxicants; formulation of non-defective topological isomerases in extended systems, with applications on graphenes as nanosystemic support for cosmetic compounds; formulation of spectral inverse quantum algorithm for extracting the information of particle/wave type in mesosystems obtained through the technique sol-gel, spectral analyzed. These models will be further unified and integrated applied to the chemical bond in orthogonal space of reactivity-activity in the last stage of the project, 2013.

Written and communicated papers (the members of the grant are in bold)

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7. **Putz M.V., Mingos D.M.P.** (Editors) APPLICATIONS OF DENSITY FUNCTIONAL THEORY TO CHEMICAL REACTIVITY Springer Structure and Bonding, Vol. 149, VIII + 224 p., 77 illus., 32 in color (2013) ISBN (Hardcover): 978-3-642-32752-0; URL: <http://www.springer.com/chemistry/inorganic+chemistry/book/978-3-642-32752-0>
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17. Ori O., **Putz M.V.** Isomeric Formation of 5/8/5 Defects in Graphenic Systems. Fullerenes, Nanotubes and Carbon Nanostructures, MS ID FNCN12101.R1/06.11.2012 accepted. **(ISI Impact Factor ~0.8)**
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