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Perspective

THEORETICAL AND COMPUTATIONAL CHEMISTRY IN TIMIȘOARA – PAST, PRESENT, FUTURE

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ABSTRACT

Research in theoretical and computational chemistry is performed in Timişoara mainly at the Chemical Research Institute and at the Chemistry Department of the West University. The main research directions are quantum chemistry-molecular orbital theory applied to organic molecules and transition metal complexes and quantitative chemical structure-biologic activity relations. The main achievement is the minimal steric difference method for QSAR type relations. Results obtained within these directions are described as well as achievements of a more theoretical physics oriented group of quantum chemists. Perspectives for future developments are also discussed.

1. INTRODUCTION

Timişoara, a city with beautiful civil engineering achievements since the time of the Austro-Hungarian rule, became a university center just after 1920 along with the establishment of the Polytechnic School, with Traian Lalescu being the first rector [1]. The Royal Decree no. 4822 of November 15, 1920 approved the establishment of the Polytechnic School of Timişoara. The city receives a strong influx of scholars during 1940-1945, with the refuge in these parts of the University of Cluj. This caused a strong stimulus for further development of the university and the academic life in western Romania, in the town located on the Bega River. July 29, 1948, marks the establishment of the Faculty of Industrial Chemistry, while the year 1951 - the establishment of the Timişoara branch of Romanian Academy and its Institute (Center) of Chemistry.

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Remarkable efforts were made by academics Ilie Murgulescu and Coriolan Drăgulescu, who have continuously and efficiently supported the development of a university learning establishment and of a modern chemical research. These two prestigious personalities of Romanian chemistry and science are recognized founders and leaders of the higher education in chemistry and of the chemical research in this part of the country. Theirs is the main merit, the decisive contribution to the establishment in 1960, inside the 3-years Pedagogic Institute, of the Department of Physics-Chemistry and later, in 1967, of the Departments of Inorganic Chemistry and Organic Chemistry at the Faculty of Physics of the University of Timișoara. The university specialization of Physics-Chemistry was abolished a few years later, following obtuse politics, abusively applied to the chemical university education from Timișoara. The specialization was re-established in 1990 at the West University of Timișoara, Faculty of Chemistry, Biology, Geography. In this new faculty, a center of excellence and a "Chemistry of Biologically Active Compounds" master studies specialization were created, a second QSAR research pole of Timișoara, along with that from the Institute of Chemistry of Romanian Academy.

With his vast professional experience, prof. I.G. Murgulescu was directly involved in developing and modernizing the course, the laboratory and the research topics in the field of physical chemistry. It can be said that during the years he taught the physical chemistry course at the Faculty of Chemistry of Polytechnic Institute Timişoara (1948-1949), prof. I.G. Murgulescu introduced the fundamentals of modern physical chemistry in Romania, which he has developed and strengthened in the coming years, with the help of brilliant collaborators whom he trained and promoted with utmost stringency.

A first line of research promoted by I.G. Murgulescu in Timișoara's group, in the field of theoretical chemistry, was the study of the influence of solvent on the kinetics of some chemical reactions. We mention here the study of the influence of solvent on the Menshutkin reaction kinetics (Ștefan Popovici and Mariana Pop [2]). It is worth mentioning the research in the field of chemistry nomenclature done by Professor Giorgio Ostrogovich (unfortunately unpublished) and those of D. Purdela concerning the theory of chemical shifts of the ^{31}P in the nuclear magnetic resonance spectrum [3]. We also note the research done by the Inorganic Chemistry team, led by acad. C. Drăgulescu and then by Dr. Septimia Policec, crowned with the publication of two reference treaties, written in collaboration with Emil Petrovici. The first, entitled "*Introducere în chimia anorganică modernă*" ("*Introduction to modern inorganic chemistry*") brings a systematic exposition of the atomic structure based on quantum mechanics and an explicit qualitative presentation of the chemical bond within the molecular orbital and the ligand field theories. The second treaty, "*Chimie structurală modernă. Chimia coordinanței 8*" ("*Modern structural chemistry. Eight-coordination chemistry*") is a work that systematizes, by its own concept, a bibliographic material of high theoretical and applied interest regarding the ligands of coordination 8. Both treaties currently maintain their timeliness.

Currently, the main centers where research in the field of theoretical chemistry is done are the Institute of Chemistry Timișoara of Romanian Academy, called here ICT, and the chemistry departments of the West University and of the Faculty of Industrial Chemistry and Environmental Engineering. In what follows, we describe the main achievements in this area.

In this time of beginnings, we mention the late Dr. Radu Vâlceanu (1923-1996), who was incorporated in 1954 at the Scientific Research Base from Timişoara. Promoted to university professor, he has emerged as one of the main animators, with major organizational and scientific contributions in the field of organophosphorus compounds. The book he designed, together with D. Purdela, "*Chimia compuşilor organici ai fosforului şi a acizilor lor*" ("*The chemistry of organic compounds of phosphorus and their acids*"), also translated into Russian, became and remains a valuable source of documentation for training dedicated specialists. At the suggestion of R. Vâlceanu, from 1972, the research undertaken by the QSAR Group was initiated and developed, targeting theoretical and practical contributions regarding the toxicity of organophosphorus compounds and, in particular, of the organophosphorus pesticides.

2. PROBLEMS AND ORGANIZATIONAL STRUCTURES

Systematic works of quantum chemistry (and, in general, theoretical chemistry) occurred in Timişoara in 1966, with the hiring of one of the authors of this paper at the Centre for Chemistry of the Scientific Research Base of Romanian Academy (see also the interesting article by Septimia Policec [4]). The main researchers involved were Zeno Simon, Radu Vâlceanu and Aurel Balint, followed, in 1968, by Mircea Mracec, and several years later, by Ion Moţoc and, especially after 1990, by Ludovic Kurunczi. After many organizational changes in the Ceauşescu era, this center was transformed into the Institute of Chemistry Timişoara of Romanian Academy since 2001, as it is known today. It is worth recalling the directors: Acad. Coriolan Drăgulescu (until 1977), Dr. Radu Vâlceanu (1977-1990), Dr. Walter Schmidt, Dr. Mircea Mracec and, currently, Dr. Otilia Costişor.

Among the participants from the West University, Department of Chemistry, we mention Adrian Chiriac and, from 2005, M.V. Putz from the Faculty of Industrial Chemistry (Polytechnic Institute Timişoara), F. Kerek and D. Ciubotariu, from the Institute of Medicine Timişoara (today "Victor Babeş" University of Medicine and Pharmacy), G.I. Mihalaş and T.I. Oprea. Access to computers, even relatively primitive, found in Timişoara during 1970-1990 (not exactly on legal basis, but more based on "begging",) is in particular due to the collaboration with S. Holban and, not the least, the continuing collaboration with A.T. Balaban (Institute of Atomic Physics (IFA) Bucharest), to which it was later added the one with Ion Niculescu-Duvăz (Institute of Oncology Bucharest), these being of inestimable value through competent criticism and through the facilitation of access to foreign publications.

Obtaining the approvals for publication in foreign journals was a difficult issue in the Ceauşescu era. We were lucky with the understanding of open minded rectors - N. Stanciu and C. Popa from University of Timişoara, and G. Băcanu from the Institute of Medicine from Timişoara. This made possible the emergence of a book [5] written in collaboration with A.T. Balaban, published at the Springer Verlag publishing house, and of a book published in the UK.

Especially in the early years, there was a fairly marked interest for quantum chemistry. A series of informal lectures was also held, for those interested. We self-proclaimed ourselves the QSAR and Quantum Chemistry Group, but without being formalized, and the Annals of West University, Series of Chemistry became a sort of unofficial press of the group. There were no difficulties, probably also due to links with the bodies concerned, held by some

members of the group - links which were by then mandatory for those who occupied a higher hierarchy.

The continuing emergence of Preprints in the Series of Chemistry at the University of Timișoara (reviewed in Chemical Abstracts) allowed the QSAR Group to be known worldwide, to be given priority for the MTD method and, as a result, to be often quoted in the dedicated literature.

After 1990, at the Department of Chemistry, Faculty of Chemistry, Biology, Geography of the West University, there is a quantum chemistry course held many years by our colleague Mircea Mracec, while for master studies – a QSAR course, held many years by Z. Simon, also with some lessons taught by T.I. Oprea (then working at AstraZeneca, Sweden), and by other colleagues with expertise in specific areas.

3. THE MAIN RESEARCH DIRECTIONS

The first issue of theoretical chemistry systematically addressed was applying the molecular orbital theory in the simplistic Hückel (HMO) variant to issues of electronic spectra and reactivity of organic molecules. Among the areas covered we mention:

- conjugated systems with tetracoordinated pentavalent phosphorus atom: A. Balint, Z. Simon, R. Vâlceanu and other collaborators;

- electronic spectra of dyes derived from 2,5-bis-phenylamino-1,4-benzoquinone, with A. Balint as the main protagonist.

More advanced quantum chemical methods could be addressed with the arrival of M. Mracec (a product of V.E. Sahini's quantum chemistry school of Bucharest) in this group. The problem was the access to modern computers. Ceaușescu era was less encouraging for this type of research.

With the reorganization of the Centre of Chemistry (which becomes ICT) after 1989 and through the energetic interventions of the directors M. Mracec and, especially, Otilia Costișor, the computing power has increased greatly. This allowed the quantum chemistry group consisting of M. Mracec, Mioara Mracec, Liliana Păcureanu and others to address more efficient methods, such as MNDO, PM3, SCF/3-21G* and even methods for molecules and ions in aqueous solution such as DFT+PCM [6].

Another line of research, probably with the highest success, was the study of chemical structure-biological activity relationships (QSAR), addressed through the initiative of R. Vâlceanu shortly after 1970. At that time it was a big problem for QSAR to include the spatial structure of the molecules in the respective relationships. This was a success of the QSAR group represented by Z. Simon, A. Chiriac, I. Moțoc, S. Holban and others, by creating the minimum steric differences method, or MSD, and then the perfected version, MTD (see [5], chapters 4 and 5, and [7]).

The last development of MTD is the MTD-PLS method [7]. Here, besides the spatial structure of the molecules, described by occupation or non-occupation of the hypermolecule nodes, six parameters also intervene that characterize intermolecular forces (fragment volume, polarizability, partial electrical charge etc.). The number of variables involved in this type of QSAR, higher than the number of molecules considered for QSAR, required the switch from using the multiple linear correlation method to the "Partial Least Squares" (PLS) method.

From the group of theorists, Simona Funar-Timofei addressed a systematic application of the techniques used in QSAR to the study of substantivity of a large number of dyes on cellulose fibers [8]. Here, the dye is analogous to the ligand, while the textile fiber resembles the receptor. This type of application of QSAR techniques is practically a world premiere, receiving a huge number of citations in the dedicated literature. The paper [9], which has 46 non-self-citations, is the most cited work of our group.

A last major issue addressed by the group of theorists from ICT is the application of quantum chemistry to aspects of ligand-receptor interaction. We mention here the calculation of conformations energy for molecules with ligand character (Mircea Mracec and Mioara Mracec); calculating the energy of dissociation (more specifically, ΔG_d) in an aqueous solution of some complexes of ML_2 type (M: Ca^{2+}, Mg^{2+}; L: ethanediol, dioxane, acetate etc.) related to a study of the peptidoglycan interaction specificity (L. Sayti, V. Careja, Simona Muntean); also, the pairing energy calculations for aqueous bases of Watson-Crick type (Lily Păcureanu, L. Kurunczi) [6, 10].

It is worth mentioning that, in the work done, semi-empirical calculations involving intermolecular potentials gave results more consistent with the experimental data (where they do exist) than ab initio calculations, in which the end result is a small difference between two large numbers [6, 11].

A separate group of theoretical chemists is led by M.V. Putz. Its approach is closer to the theoretical physics than that of the group at ICT. Among the many researched topics prevail those related to the definition of electronegativity by density functionals (e.g., see [12]), although QSAR related topics are also present. Putz and his collaborators have published more than 80 primary papers and reviews, with over 120 citations in the dedicated literature.

4. CONCLUSIONS AND PERSPECTIVES

The main groups concerned with theoretical and computational chemistry from Timișoara are those from ICT and from the West University (M.V. Putz). The ICT group elaborated hundreds of papers in the field of computational chemistry and, in particular, related to its application in spectra, reactivity and biological activity, and dye-fiber substantivity. There are many hundreds of citations of its publications in the dedicated literature. The main achievement is related to the steric factor in the biological activity, the MTD method of structure-property relationships and the biological activity. Quantum chemistry methods were also used in these studies.

The group from the West University (led by M.V. Putz) operates from less than 10 years and will probably bring many contributions to theoretical chemistry.

Over time there have been numerous collaborations of the ICT group with research groups with similar interests at home and abroad, the most important being that with T.I. Oprea's group from New Mexico. There have also been important exchanges of researchers with groups from abroad; unfortunately, together with departures and expatriations, as is the case with many other research groups in Romania. The causes of this "brains loss" were much discussed in this journal. It is worth mentioning, related to the Timișoara university center, a collaboration - bound to grow stronger, between the Medicine in Timișoara and its counterpart from Szeged. This collaboration also has implications in the drug design and the QSAR fields.

A larger infusion of funds into research would be required for the "brains" exchange to take place in both directions. The problem is ultimately linked to the overall economic development of Romania and this paper is not the place for a broader discussion on this topic.

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