

# MATHEMATICAL AND COMPUTATIONAL CONCEPTS IN CHEMISTRY

*Editor:*

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Published for the  
INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY



ELLIS HORWOOD LIMITED  
Publishers Chichester

Halsted Press a division of  
JOHN WILEY & SONS  
York Chichester Brisbane Toronto

First published in 1986 by

**ELLIS HORWOOD LIMITED**

Market Cross House, Cooper Street, Chichester, West Sussex, PO19 1EB, England

*The publisher's colophon is reproduced from James Gillison's drawing of the ancient Market Cross, Chichester.*

**Distributors:**

*Australia, New Zealand, South-east Asia:*

Jacaranda-Wiley Ltd., Jacaranda Press,

JOHN WILEY & SONS INC.,

G.P.O. Box 859, Brisbane, Queensland 4001, Australia

*Canada:*

JOHN WILEY & SONS CANADA LIMITED

22 Worcester Road, Rexdale, Ontario, Canada.

*Europe, Africa:*

JOHN WILEY & SONS LIMITED

Baffins Lane, Chichester, West Sussex, England.

*North and South America and the rest of the world:*

Halsted Press: a division of

JOHN WILEY & SONS

605 Third Avenue, New York, N.Y. 10158 U.S.A.

©1986 International Union of Pure and Applied Chemistry IUPAC Secretariat:  
Bank Court Chambers, 2-3 Pound Way, Cowley Centre, Oxford OX4 3YF, UK.

**British Library Cataloguing in Publication Data**

Applications of mathematical concepts to chemistry.

1. Chemistry- Mathematics

2. Numerical calculations

I. Trinajstić Nenad.

II. International Union of Pure and Applied Chemistry

III. International Symposium on Applications of Mathematical

Concepts to Chemistry (1985-Dubrovnik)

540'.1'51 QD39.3.M3

ISBN 0-85312-934-7 (Ellis Horwood Limited)

ISBN 0-470-20289-0 (Halsted Press)

Printed in Great Britain by Butler and Tanner, Frome, Somerset.

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Based on the invited and special lectures presented at the International Symposium on Applications of Mathematical Concepts to Chemistry, Dubrovnik, Croatia,

September 2-5, 1985

Symposium was sponsored by IUPAC, Union of Chemical Societies of Yugoslavia, The Croatian Chemical Society, and Department of Physical Chemistry in the Rugjer Bošković Institute, Zagreb

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This book is dedicated to great Croatian scientists

Rugjer Bošković (1711-1787)  
Andrija Mohorovičić (1857-1936)  
Lavoslav Ružička (1887-1976)  
Božo Težak (1907-1980)

## Preface

Chemistry in general and chemical thermodynamics in particular. We accepted the responsibility, both as an honour and a privilege. We are especially happy that the long standing tradition of Mathematical Chemistry in this country, and in Croatia in particular, has been recognized in this way. Hence, this the first symposium dealing exclusively with topics that constitute Mathematical Chemistry has been organized by our Group with great fervour and enthusiasm.

We selected Dubrovnik as the site of the symposium because it is one of the most interesting Croatian cities with a distinguished historical, cultural and scientific heritage. The famous Croatian scientist Ruđer Bošković, fellow of the Royal Society (London), Professor of Main Lines at Collegium Romanum in Rome, and founder of the Observatory at Brijuni, was born here (May 18, 1707). Besides Dubrovnik, known for its mild Mediterranean climate, is a frequent site for scientific meetings, and is easily accessible by land, sea and air.

The International Symposium on the Applications of Mathematical Concepts to Chemistry was attended by 121 participants from 21 countries. The Symposium brought together mathematical chemists, computer chemists, theoretical chemists, mathematically and theoretically minded experimental chemists, mathematical physicists and mathematicians, for discussions about the status of Mathematical Chemistry, its perspectives, and its influence on various aspects of Chemistry.

Last day of the Symposium has been dedicated to the memory of the late Professor Andrej Azman (Celje 1937 - Ljubljana 1980) who in his time was the leading chemical theoretician in Yugoslavia and inspiring supporter of Mathematical Chemistry. Last, but not least, during the Symposium important preliminary steps have been made to establish an International Society of Mathematical Chemistry. We expect that the combination of exciting science, beautiful scenery, warm weather and the hospitality of the local people made the Symposium a memorable experience for all participants.

The lectures and posters covered a significant part of the broad spectrum of problems in Mathematical Chemistry and its interactions with other areas of Chemistry. The Symposium also revealed the permanent need for Mathematics in all branches of Chemistry. In addition, it became evident that Mathematical Chemistry will continue to grow as a part of

## Preface

Theoretical Chemistry; other overlapping but distinguishable parts include Quantum Chemistry, Statistical Mechanics and Computational Chemistry.

The contributed papers presented at the Symposium will appear in a special issue of *Croatica Chemica Acta*, a chemistry journal published by the Croatian Chemical Society.

Zagreb, September 1985.

Nenad Trinajstić

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# INTRODUCTORY REMARKS

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About 200 years ago Immanuel Kant wrote in his "Kleinere Schriften zur Naturphilosophie": "Ich behaupte, dass in jeder besonderen Naturlehre nur so viel Wissenschaft angetroffen werden könne, als darin Mathematik anzutreffen ist". He wrote then: "Solange also noch für die chemischen Wirkungen der Materien aufeinander kein Begriff aufgefunden wird, der sich konstruieren lässt ....eine Forderung, die schwerlich jemals erfüllt werden wird - so kann Chemie nichts mehr als Kunst oder Experimentallehre, niemals aber eigentliche Wissenschaft werden". Just about the same time Lavoisier was introducing mathematics into chemistry through his use of the balance. The law of definite proportions became the basis of stoichiometry and every chemist-artist had to learn some arithmetic.

The next great step in development of chemistry was the structural theory, but the pioneers in this field, Butlerov, Couper and Kekulé did not realize that the structural formulae are actually mathematical objects, graphs. It was the mathematician Arthur Cayley who first became aware of that and he developed the theory of tree-graphs by trying to calculate

the number of possible constitutional isomers of paraffin hydrocarbons  $C_nH_{2n+2}$ . Later, Georg Polya, in an encounter with problems of isomerism discovered his famous theorem which became one of the fundaments of combinatorics. These mathematical achievements, however, had very little impact on the daily praxis of chemists, because their everyday problems were usually so simple that they could mostly be solved by trial and error.

Soon after the structural theory had been developed Jacobus Hendricus van't Hoff and Achilles Le Bel founded organic stereochemistry and Alfred Werner the stereochemistry of inorganic complexes. Symmetry, dissymmetry and asymmetry became recognized as important features of molecules, and although group theory was clearly the branch of mathematics most appropriate for treating problems in this area very few chemists made use of it.

The gate of entrance for more sophisticated mathematics into chemistry was and still is physical chemistry. Step by step, methods of mathematical physics penetrated into chemistry: first calculus, to deal with problems of chemical thermodynamics and kinetics, then linear algebra and group theory, as additional tools of quantum chemistry and molecular spectroscopy.

The more recent general impact of computers on chemistry and on chemists cannot be overestimated. Without computers theoretical chemistry, structural analysis by diffraction methods, molecular mechanics, etc. could not have developed far, and the collection, retrieval and classification of the terrifying multiplicity of chemical data would be almost impossible. The design of syntheses and analyses of reaction pathways are other promising applications.

Last but not least topological aspects of chemical concepts such as e.g. aromaticity, should be mentioned. Thus the progress of chemistry depends more than ever on applications of mathematics.

The important aims of such conferences as this one are to bring together scientists who use the many different branches of mathematics in chemistry and to bridge existing gaps between them, to learn about the new work of pioneers and about the progress in estab-

lished fields. The titles in the programme indicate that almost all mentioned topics will be covered.

In summary one can say that chemistry today includes quite enough mathematics to be considered a respectable science from the Kantian point of view, but let us also not forget what Lord Kelvin said about physics: "It is as dangerous to let mathematics take charge of physics as to let an army run a government."

## Chapter 2

# THE MATHEMATICAL TRAINING OF CHEMISTS

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I was recently a member of an appointing committee for a university lectureship in mechanical engineering and was struck by the fact that none of those interviewed had dirty fingernails. I should put it less glibly: everyone that was seriously considered for the post was involved in the computer simulation of structures rather than the building and testing of rigs. Of course, one can understand why this is so: it is far cheaper to do a computer simulation of an oil rig than to build one and test it to destruction. I assume that somewhere in the background there must be engineers with oily hands who are still building and testing, because one can only confidently use mathematical models to extend empirical knowledge by small amounts. Nevertheless, the balance between the mathematical model builders, and the rig builders and testers, seems to have swung far towards the clean handed people in recent years.

I do not think this situation has occurred yet in chemistry which is still predominantly an empirical subject. In fact, I would go as far as to say that the mathematical models used in chemistry still have rather poor predictive performance. How often does an experimental chemist ask for the results of a calculation before deciding whether an experiment is likely to prove fruitful? In part this is

because chemical experiments are still generally cheap and not too time consuming. It is quite often quicker to do a good experiment than a poor calculation.

However, the situation is bound to change in the future and one can see already that this is beginning in some of the more expensive fields such as the pharmaceutical industry. It costs several million pounds to bring a new drug to the market so that any model which can narrow the field of likely candidates is very useful.

The point of this preamble is to stress that what has in the past been found adequate by the chemical community for their models may not be adequate for the future. I am not saying that our chemistry courses should ignore the Friedel-Craft's reaction in favour of more time for the Schrödinger equation. Rather that we should move our theoretical studies a little away from conceptual models towards more quantitative models.

I have for many years been struck by the fact that chemists and physicists seem to have different approaches to theoretical problems. Physicists like to solve approximate models exactly and chemists prefer to solve good models approximately. Think how far the physicist has gone with the particle-in-a-box. In fact, I believed that most physicists are by training or inclination even less inclined to seek the help of quantitative mathematical models than are chemists.

You might justly ask whether I practice what I preach. Well, with my close colleagues Sydney Kettle and John Tedder I have written two undergraduate textbooks on the theory of the chemical bond. The first of these, Valence theory, was written in 1965 and is quite firmly based on mathematical skills. For example, the book shows how to derive the ligand field matrix for  $p^2$  in the intermediate (weak-strong) coupling regime, which I think is quite tough for an undergraduate text. We assumed that the reader had a prior knowledge of vector, operator and matrix algebra and possessed a spirit which was not overawed by mathematical manipulations. However, Valence theory is essentially a book that deals with concepts. In a later edition we derived the Hartree-Fock-Roothaan equations but there were few references to the results which could be obtained from them.

Our second book, The Chemical Bond, was published in 1978 and is much less mathematically demanding; nothing more is required than the ability to expand a secular determinant.

However, the principles underlying the ab-initio SCF approach are explained and the results of such calculation are used to establish the validity of the qualitative MO approach. For example, the concept of a molecular orbital is developed not only by arguments based on the LCAO approximation but also by examining the actual ab-initio results for  $H_2^+$ . Our view in 1978 was that students could appreciate the basis of quantitative calculations without having the mathematical ability to follow the problems encountered in, say, integral evaluation. In a new edition of the book, soon to appear, we are more expansive on the mathematical basis of the ab-initio method and on the general structure of the commonly available black-box SCF programs. I stress my belief that one can get students to understand the basis of the ab-initio method and to appreciate the results of such calculations even though their mathematical background is poorer than is required to follow many of the conceptual models of valence theory.

We have been struggling for many years to produce students who are literate and numerate. We should now also require them to be computerate. I do not much like the word but I am sure it will not be long before it appears in the Oxford English Dictionary.

I had originally intended to start this essay with a list of the mathematical tools that all chemists should know. On further reflection I decided that was not very useful. I am sure that most of us would take the view that almost any mathematical skill can be valuable. Putting this the other way round: I would be most reluctant to pick out any mathematical topic as being unworthy of study or as being of no use to chemists. The reason that we are at this conference rather than the Burgenstock conference on Natural Products (I know a few of us go to both) is not that we know a great deal of mathematics but that we have an appreciation for the mathematical approach. I would even say that most of us would find some joy in the proof that the square root of two is not a rational number - and I cannot think that has much relevance to theoretical chemistry.

However, I will finish by telling you what mathematics is known by one of our most eminent organic chemists. I told Professor John Cornforth that I was to give this talk and in order to see what was the minimum requirement for a good organic chemist I asked for the things he knew. This was his list:

- (i) Elementary arithmetic
- (ii) Two-dimensional geometry including analytical

- geometry
- (iii) Plane trigonometry and trigonometric functions
- (iv) Conic sections
- (v) Elementary algebra
- (vi) Simultaneous equations
- (vii) Permutations and combinations
- (viii) Differential calculus
- (ix) Integral calculus
- (x) Differential equations (including partial)
- (xi) Theory of probability
- (xii) Theory of errors
- (xiii) Exponential functions
- (xiv) Binomial theorem

He regretted not knowing:

- (i) Prime numbers
- (ii) Diophantine equations
- (iii) Topology
- (iv) Symmetry

Well, I suspect we do not have a typical case here. I am certain that if he had sought my opinion on what organic chemistry a theoretician needed to know my list would have been much less impressive.

## Chapter 3

# THE EFFECT OF ELECTRO-NEGATIVITY ON BOND LENGTHS IN MOLECULAR MECHANICS CALCULATIONS

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## ABSTRACT

The attachment of an electronegative atom or group to a carbon-carbon bond causes that bond to have a reduced length. The magnitude of the reduction is roughly proportional to the electronegativity of the attached atom. The substitution of multiple electronegative atoms on the same bond leads to a further reduction of the bond length, unless the size and number of the groups is sufficient so that steric effects outweigh the electronegativity effect. Carbon-hydrogen bonds and carbon-halogen bonds behave similarly, except that the degree of shrinkage differs, depending upon the particular bond. Attachment of an electropositive atom causes a bond lengthening. Within the context of molecular mechanics, these changes in bond length occur in the "natural bond length", or  $l_0$  value for the bond, and whatever other effects may be present in the bond due to its particular environment also occur as usual, giving a resulting bond length which may be smaller or larger than the usual value by as much as 0.050 Å or so.



## INTRODUCTION

The energy of an electron in a 2s orbital on carbon is much lower than that of an electron in the corresponding 2p orbital. Hence, if a hydrogen atom in an alkane is replaced by an electronegative atom, the carbon bonded to that electronegative atom responds by donating electron density to the electronegative atom, which means the bond to that atom contains more p character than it did in the alkane. If one bond to a carbon has the amount of p character in it increased, the other bonds to that carbon must between them have an increased amount of s character. Considering carbon-carbon bonds in general, an increase in s character (from an  $sp^3$  hybridization) will give a shorter bond, while increased p character will give a longer bond. Thus the attachment of an electronegative atom in, say, ethane, to give fluoroethane, yields a molecule with a shorter carbon-carbon bond than in ethane itself. And attachment of an electropositive atom would yield a longer carbon-carbon bond, for analogous reasons. Experimentally these changes in bond length have long been known, as has the interpretation given.<sup>1-5</sup>

The molecular mechanics treatment of hydrocarbons has been worked out in considerable detail. While it cannot be said that all problems have been solved in this area, most of them have been, at least to a reasonably good approximation. Thus for ordinary saturated hydrocarbons, one can calculate good structures by what are now standard methods.<sup>6</sup>

When one adds other atoms onto the hydrocarbon framework, then the situation is somewhat different. Depending on the type and number of the substituents on the hydrocarbon, the geometries as now calculated by molecular mechanics may be appreciably in error. Since most organic molecules contain various kinds of functionalized substituents, it is also important to be able to deal with the effects of these substituents accurately.

We have been interested in refining the MM2 force field<sup>7</sup> so as to obtain more accurate structures for functionalized molecules. As a prelude to this, we gathered a large amount of representative experimental data so as to quantitatively study this electronegativity effect. We have also carried out ab initio calculations on this effect, and in particular on the torsional dependence of the effect. Some of these calculations have been published previously.<sup>8</sup>

As far as molecular ground states, theory and experiment show substantially the same thing, namely that a given bond will be shortened if an electronegative atom or substituent is attached to it, and lengthened if an electropositive atom is attached to it.<sup>1-5,8</sup> The amount of shortening or lengthening is roughly proportional to the electronegativity of the