

Chemistry is traditionally an experimental science. However, recent advances in computer technology and the development of highly efficient computer algorithms have opened the way for a viable alternative approach to chemistry: chemistry by computer. We use such computer calculations to determine the structures of molecules and to help understand how molecules react with one another. The procedure employed is called *ab initio* molecular orbital theory, the term *ab initio* signifying that the calculations are carried out from first principles using the laws of quantum mechanics. No experimental data other than values of fundamental physical constants are used. An important feature is that the calculations can be carried out as readily for reactive or hazardous species as for normal, stable molecules. They are therefore particularly useful in cases where experimental studies might be difficult or impossible. Properties that may be examined include molecular structures and reaction pathways, as well as many thermodynamic and spectroscopic properties.



During the year, we enjoyed stimulating interaction with a number of visitors. Thomas Büsgen, an undergraduate student from the University of Applied Sciences, Bonn-Rhein-Sieg, spent five months in the group, funded by the Studienstiftung des Deutschen Volkes. Ines Corral, a visiting PhD student from the Autonoma University of Madrid, joined the group for three months in September, on a fellowship funded by the Ministerio de Educación, Cultura y Deporte of Spain. Most recently, Dr Maya Topf from the University of Oxford and Professor Uri Zoller from the University of Haifa joined the group as Visiting Fellows in October and November. In addition, Dr Rodolfo Gomez-Balderas joined the group in February after having won a Fellowship funded by the Consejo Nacional de Ciencia y Tecnologia of Mexico, while Dr Michelle Coote took up an ARC Postdoctoral Fellowship in the group in June.

Enzyme-catalysed Reactions

Vitamin B₁₂ is one of nature's essential vitamins. We have used *ab initio* calculations to model reactions mediated by coenzyme B₁₂. Although these reactions have been extensively studied experimentally, there is certainly no consensus as to how they proceed. We find that protonation and/or deprotonation at appropriate sites facilitates the reactions, and that reactions that are facilitated by protonation (or deprotonation) are facilitated by the partial-proton-transfer that enzymatic hydrogen bonding can provide. Our most recent studies have been directed at the reaction catalysed by the enzyme ethanolamine ammonia lyase where we find that interactions between the enzyme and the migrating group of the substrate that afford an almost fully-protonated migrating group will lead to the most efficient catalysis. This and other recent examples provide strong encouragement for the use of computer calculations in a predictive manner in the study of enzyme reactions. (with M.L. Coote, J.T. Bennett, and B.T. Golding [U. Newcastle upon Tyne], D.M. Smith [Ludwig Maximilians U., Munich], S.D. Wetmore [Mount Alison U., Canada])

Development of Improved Theoretical Procedures

The ability to predict reliable thermochemistry represents a very important application of *ab initio* molecular orbital theory. We have recently been

designing and assessing methods that are suited for predicting accurate thermochemistry for free radicals because these represent particular challenges for theoretical investigation. Our latest work has been concerned with methods that we have designated G3-RAD, G3X-RAD, G3(MP2)-RAD and G3X(MP2)-RAD. (with D.J. Henry, M.B. Sullivan)

Free Radical Chemistry

Radicals are ubiquitous in chemistry, biology, and polymer science. Because they are reactive species, they are often difficult to study experimentally and therefore theory has a potentially useful role to play in their characterisation. We have been using theory to determine radical stabilisation energies, with the important aim of seeing how individual substituents stabilise or destabilise a radical centre. We have also been examining the details of radical addition reactions and radical abstraction reactions, both of which are very important in biological chemistry and polymer chemistry. A particularly important application is concerned with gaining a better understanding of the RAFT polymerization process with the ultimate aim of improved process control. (with M.L. Coote, D.J. Henry, R. Gomez-Balderas, G.P.F. Wood, and H. Fischer [U. Zurich], M.W. Wong [U. Singapore])

Oxidative Damage to Proteins

An understanding of the oxidation of proteins by free radicals is of great importance because of its implication in a number of human disorders such as Alzheimer's disease, atherosclerosis, and diabetes, as well as aging. We have been using *ab initio* molecular orbital calculations to address the problem. Initial targets have included the cleavage of the peptide backbone following radical formation, and migration of the radical site within the peptide. (with G.P.F. Wood, M.L. Coote, R. Jacob, C.J. Easton, and M. Davies [Heart Research Inst., Sydney], R.A.J. O'Hair [U. Melbourne], A. Rauk [U. Calgary, Canada])

Oxides and Hydroxides of Alkali and Alkaline Earth Metals

We have been examining the alkali metal oxides and hydroxides as a preliminary to investigating their interesting acid and base properties. Reliable experimental data are very sparse for these molecules. Their theoretical description is not entirely straightforward either and has necessitated incorporation of several new features and the development of new basis sets. (with M.B. Sullivan, A.P. Scott, T. Büsgen, and B.J. Smith [Walter and Eliza Hall Inst., Melbourne], J.M.L. Martin [Weizmann Inst., Israel], L.A. Curtiss [Argonne Nat. Lab., USA], S.R. Kass [U. Minnesota, USA])

Hydrogen Bonding

Hydrogen bonding is of great importance in chemical and biological systems. Previous studies have mostly focused on hydrogen bonds involving electronegative elements, e.g., O—H•••N. We have examined instead the weaker hydrogen bonds to carbon, e.g., C—H•••N. We have carried out systematic studies aimed at identifying which types of systems will exhibit the strongest C—H•••X hydrogen bonds. The effect of electronegative substitution has been particularly targeted. (with S.D. Wetmore [Mount Alison U., Canada])

<http://www.rsc.anu.edu.au/radom.html>