Professor Jim Coxon
A Tribute

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His research work has generated more than 200 publications, including authorship or editorship of many books and review articles. His books include "Principles of Organic Synthesis" with the late Professor Sir Richard Norman and its complementary volume "Worked Solutions in Organic Chemistry," written after Sir Richard's death, with Associate Professor Juliet Gerrard. His first book "Organic Photochemistry" was co-authored with Professor Brian Halton. His contribution to the university has included a term as Dean of Science and he is now a member of the University Council, the Governing Body of the University.

Following the appointment of the late Professor David Kirk to Canterbury, a strong steroid school developed involving collaboration between Professor Michael Hartshorn and Jim Coxon, which continued after Professor Kirk's return to the UK. Many steroid rearrangements were discovered and experiments carried out to understand the details of these reactions. With the recognition of the importance and spectacular nature of the spinal rearrangement of steroids came the need for model studies to understand these processes. Experiments with deuterium labelled compounds established the stereochemistry of 1,2-elimination and 1,3-elimination with rearrangement in decalin systems, which modeled the steroid framework. The studies showed the anion and its mobility to be important, since it acts as base in the removal of a proton in each process. The relative rate of conformational change compared with elimination was established and kinetic isotope measurements were made.

A long-standing interest in the chemistry of small ring compounds originated from studies of steroid epoxides. The strain of the three membered rings, on reaction with acid, was used to induce skeletal change. This led to the discovery and rationalization of diastereotopic selection in the rearrangement of methylene epoxides - one of the first examples of the use of a deuterium label to measure the relative rates of processes faster than the rate-determining step of the reaction. The work included an investigation of the involvement of proximate functional groups on the course of reaction and demonstrated unique aspects of molecular gymnastics of bifunctional molecules. Jim continues his studies in this field.

An early discovery that both the proton and mercuric ion attack at the corner of cyclopropanes led to work carried out at Canterbury and Florida with Professor Merle Battiste. These collaborative studies had relevance to the mechanism of alkyl migration, and advanced the understanding of this fundamental process in organic chemistry. The explanation offered for the electrophile trajectory is now accepted. A series of papers followed involving *ab initio* calculations to gain insight into the potential energy surface of the reactions.

A study was made on pinane thermolysis, which has had applications in the perfumery industry, and involved thermally induced rupture of the strained cyclobutane ring and the effect of substituents on adjacent bond rupture. Jim, together with former graduate student, Professor Peter Steel, also wrote a series of papers on carbocations generated in super-acid at low temperatures and studied by NMR methods. The studies (dates?) added to knowledge on the energetics of skeletal change in bicyclic systems and the relationship of proximate structure on charge distribution, one of the most controversial arguments in chemistry during that decade. The group went on to utilize super-acids in the synthesis of some novel tricyclic structures.

More than 20 years ago Jim recognized that computational chemistry would become important. He developed research in molecular modeling and *ab initio* molecular orbital calculations in advance of this field becoming fashionable for organic chemists. A sophisticated study involved the modeling of carbohydrate solution properties and was carried out by collaboration with his son, Dr Edward Coxon. Due to conformational averaging, nuclear magnetic resonance nOe data only reveals 'virtual' or 'average' conformations for flexible molecules in solution. Coincidental agreement between these virtual conformations and X-ray crystal data using oversimplified modeling studies led to the long held belief of carbohydrate rigidity. Edward's studies revealed dramatic flexibility of carbohydrates in solution, contrary to conventional understanding at that time. This is now widely accepted. Methodology to calculate correlation times of individual proton-proton vectors, and proton nOe buildup rates from molecular dynamic trajectories, were developed for comparison with experimental nOe buildup data.

At present Jim has been developing a new research topic with Professors Andrew Abell, Roy Bickerstaffe and Dr Jim Morton, aimed at the development of a medical treatment for prevention of cataracts. One of Jim's former graduate students, Dr Quentin McDonald of Q-Bit NZ, a lead developer of Macromodel, is also collaborating in this project. A library of thousands of potential inhibitors has been developed, based on the scaffold of known inhibitors by "virtual

combinatorial" methods and the best lead compounds have been synthesized for *in vivo* and *in vitro* testing. The group currently has inhibitors being tested in animal models. Adjunct Professor William Swallow, a former graduate student of Jim's, has joined the cataract project to offer management expertise on commercialization.

Jim has on many occasions spoken about how he considers himself privileged to have been associated with so many talented students and colleagues, just a few of whom have been named above. Jim has been an enthusiastic supporter of his younger kiwi organic chemistry colleagues both at the University of Canterbury and elsewhere. His colourful personality coupled with his sustained passion for organic chemistry has rendered him a superb role model for those who have been fortunate to cross paths with him either as a student, colleague or collaborator. New Zealand science, in particular, organic chemistry, owes much to this esteemed colleague.

Professor Margaret Brimble, *University of Auckland*
Professor Peter Steel, *University of Canterbury*

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