

BOOK NOTES

Explorations with Sugars : How Sweet It Was, Raymond U. Lemieux, Profiles, Pathways, and Dreams Autobiographies of Eminent Chemists, Jeffrey L. Seeman, Series Editor, American Chemical Society, Washington, D.C., 1990, pp. 186 + xx.

With each autobiographical subject that enters the reader's mind is the need to ascertain why and how the individual under consideration has arguably become one of the "movers and shakers" of twentieth century organic chemistry. Despite inevitable variation among all the authors, the vast majority do indeed share certain common qualities; capability for performing enormous amounts of work, outstanding intellectual creativity, the capacity to engender motivational inspiration, unusual leadership skills, a shrewd appreciation of the major directions in which their discipline is heading, and common decency. Almost all of the individuals emerged as dominant figures within a decade of completing their formal education. Eminence in their chosen profession of chemistry developed because all of these individuals combine a greatness of character with obvious Olympian ability. Lemieux is no exception to this analysis. Yet, beyond their shared strengths and virtues there is another aspect to these individuals - they are uniquely interesting people. There is no one else in all of science just like Raymond Lemieux. One marvels at how these autobiographical subjects, in spite of so many personal and professional qualities held in common, nevertheless, are so truly individualistic.

From incidents that took place in his youth, one is struck by the complex facets that made up Lemieux's personality. How many other tough kids from Edmonton who similarly grew up in humble circumstances would be capable, as a high school student, of independently discovering the law of Dulong and Petit while "fooling

around" with his chemistry lessons? As is so common with many other emerging scientific personalities, one sees in this teenager's pedagogical experience the future scientist's innate capacity for complex pattern recognition. At a time when other boys his age were learning to drive the family car, Lemieux was already exhibiting that very rare combination of curiosity, intellectual playfulness, and an inner need for insight into the aesthetic aspect of Nature that drives the true scientist's spirit. It was this same interest in tying together loose ends and data misfits that over and over again helped Lemieux to make extremely important discoveries. How many other chemists in trying to empirically fit together proton NMR spectra would have, with hardly a shred of theoretical scaffolding as a basis, been willing to propose negative coupling constant signs to fit their data? How many academic or industrial chemists could combine the ability to be both creative and courageous - unwilling to be discouraged from at least entertaining an unusual hypothesis until it could be replaced by something closer to the truth. Repeatedly, Lemieux juxtaposes the hard work of establishing reliable data against the need to stretch beyond the obvious in order to find a satisfying explanation for a current mystery. To borrow a phrase made popular in a contemporary American television program, Lemieux's style is always an optimistic unfolding of the simple aphorism: "The Truth is out there".

While his original interest in carbohydrates was perhaps partly due to his choice of a thesis advisor, Prof. Purves of McGill, the intellectual excitement contributed by his mentor made him a passionate convert. Lemieux eloquently describes the many fascinating discussions he and Purves had regarding stereochemistry and the structure and synthesis of sucrose, while both of them sat in Purves' office and smoked Purves' tai-

lor-made cigarettes. What better introduction to a career within science than quiet afternoons while master and disciple calmly examine in pure collegial fellowship the mysteries and complexities of the sugars?

Lemieux also gravitated to carbohydrate chemistry through a conscious decision he made on the basis that sugar derivatives play a key role in metabolism. Consequently, the study of sugars should lead to great insights into biochemistry and perhaps directly afford applications to human medicinal chemistry. While his initial investigations might best be characterized as simply meeting the unsolved needs of carbohydrate chemistry in the 1940's, the persistence and individualistic brilliance of Lemieux allowed him to revitalize the discipline. From the perspective of being attracted to organic chemistry via its direct applications to biology and medicine, Lemieux can be counted as an excellent contemporary example of the more traditional organic chemists of the 19th century. While this classical focus was somewhat deflected because of the enormous strides in mechanistic understanding, physical phenomenology, and materials science that both characterized and dominated the period from 1940-1975, a return to this biology/chemistry interface is now very much in the air. One has only to consider the thematic discoveries pouring in a constant stream out of the laboratories of such researchers as Schreiber, Boger, and Nicolaou to see numerous benefits from the marriage of organic chemistry and direct biomedical applications. For an intriguing well-reasoned commentary that touches on this intellectual repositioning (perhaps even worthy of being termed a paradigm re-shift using jargon borrowed from Kuhn), the reader is directed to the comments of Albert Eschenmoser (*Angew. Chem. Int. Engl.* 1994, 33, 2363) made for the purposes of introducing a historical essay by F. W. Lichtenthaler on the contributions of Emil Fischer.

A singular influence on the development of Lemieux's scientific style was his participation in the metamorphosis of ambitious but relatively modest institutions into world-class research operations. This certainly provided a frontier flavor to his choice of research topics as well as allowed for the attracting of a particular sort of graduate student. When resources are severely limited, ideas can become exquisitely focused thereby ensuring that the possibility of squandering time and effort along blind alleys are much less probable. One can see this in the choice of one major initial carbohydrate research goal - an efficient approach to the synthesis of glycopyranosides. After a long series of well-chosen skirmishes at the edges this problem, even-

tually sufficient experimental progress and mechanistic insights were obtained so that attack on the final objectives became possible. Thus, using one beautifully researched experimental methodology, the efficient synthesis of maltose, trehalose, and sucrose was reduced to practice. Indeed, once initiated, the actual synthesis of sucrose was achieved in a very timely fashion. Achievement of this objective was so astounding to the scientific community that it has been accorded almost the status of a chemical epiphany. For example, generations of American undergraduates who have studied from various editions of an immensely popular textbook (*e.g.*, Morrison and Boyd "Organic Chemistry", 6th Ed., Prentice Hall, Englewood Cliffs, New Jersey, 1992, p. 1192) have been intrigued, delighted, and stimulated on reading that "the synthesis of sucrose, by R. U. Lemieux of the University of Alberta, has been described as 'the Mount Everest of organic chemistry'."

As is so often the case with the authors of this autobiographical series, a fixation with stereochemical issues serves both as providing certain favored directions for their research thrust and also providing a scaffolding for relating the evolution of their research themes from one topic to the next. Extracting a point from Eschenmoser's previously cited comments, it might even be argued that much of the evolution of contemporary organic chemistry, biochemistry, and molecular biology is ultimately in the direction of supramolecular science with its strong stereochemical flavor. Prof. Lemieux's body of work is no exception.

Lemieux's early interest in relative configurations rapidly expanded into a general study of stereochemical concepts thereby making his mind unusually receptive to the emerging ideas of conformational analysis. Both historically and in a practical sense, stereochemical issues are paramount in the carbohydrates. For new levels of exploration, chemists needed ever more powerful tools to assist their interpretation of experimental results.

At the very beginning of his independent career, Lemieux examined the behavior of chemical models that straddled the cyclohexane and pyranose worlds. He looked carefully for new tools that would assist him in these endeavors and was rewarded by becoming one of the earliest synthetic organic chemists to appreciate truly the power of magnetic resonance techniques at a time in which he was both still mastering the theory and learning how to make the cantankerous early instruments perform in a satisfactory fashion. Anyone who has ever used a modern computer-controlled FT instrument in which almost everything is automatic except the brew-

ing of the spectroscopist's morning cup of coffee needs to have some sensitivity as to just how difficult it must have been in the early days. As Lemieux notes (p. 31): "I well remember when we learned that our spectra would be much improved by spinning the sample tube." From his initial experiments, there came an understanding in how to assign configurations of axial and equatorial hydrogens on the basis of both chemical shift and, more importantly, coupling constants. The ability to rapidly assess preferred conformations in solution was of enormous significance both to carbohydrate chemistry in particular and to natural products structure elucidation in general. The sophistication of NMR applications continued to increase throughout Lemieux's career eventually leading to a series of beautiful NOE experiments as well as interesting applications of deuterium influences on chemical shifts, hydrogen bonding, and exchange phenomena.

One of the most important themes in Lemieux's work is his concern with what is known as the "anomeric effect." Basically, the anomeric effect concerns the influence that heteroatoms within a cyclic system have on the most stable conformations of nearby epimeric centers. This is a very complex phenomenon that almost certainly still carries locked within itself unexpected surprises. In elementary undergraduate organic chemistry courses, students are correctly taught that substituents about a simple all-carbon cyclohexane ring are thermodynamically almost always considerably more stable when equatorial rather than axial. However, matters become much more complex when one is dealing with a cyclic system that has a heteroatom substituent present, especially an oxygen. Recognition that both the atoms within the molecule as well as atoms in the external environment exercise a major influence on the preferred geometry has been seminal. Furthermore, an understanding of the subtlety of this phenomenon has the potential of giving scientists molecular insights of even more global significance. For decades, scientists have been attempting to calculate *a priori* the folded geometry of polypeptide and protein chains. The body of published work on the geometry of glycosidic linkages in oligosaccharides, again with Lemieux one of the major contributors, provides a valuable model and numerous clues for attacking the much more difficult amide intra- and inter-molecular interactions. For Lemieux, his research has now evolved to the point where computer calculations and molecular modeling permit structure predictions even for such complex carbohydrates as the B human group trisaccharide - an outstanding achievement.

In pursuit of his scientific interests, Lemieux's research has undergone a marvelous progression from the

study of relatively straightforward organic synthetic modifications onward to the investigation of some of the most difficult unsolved mysteries of immunology. In the study of blood group determinants, enormous progress has been achieved through his collaboration with an international cast of fellow scientists. Practical biomedical applications of Lemieux's fundamental advances to the preparation of pure monoclonal and polyclonal antibodies and for the purification of blood products are of the highest rank. Lemieux has performed an elegant series of investigations into the binding of various oligosaccharides to the anti-I-Ma antibody, to lectin 1 of *Ulex europaeus*, to monoclonal anti-Lewis antibodies, and to lectin 4 of *Griffonia simplicifolia*. His excitement (and their obvious scientific importance) is inherent in his description of this work in the latter third of the autobiography. In fact, Lemieux presents a "coda" at the end of the text describing recent work involving elucidation of the molecular structure of lectin 4 at near-atomic resolution and the implications of this information in the binding properties of the molecule. Juxtaposing the coda with a picture of his family, one can appreciate a fatherly sense of pride in science well done. One cannot escape being impressed with the combination of ability and courage that has allowed Lemieux to journey from the highly circumscribed problems of simple organic transformation to an exploration of the mysteries of the vertebrate immune system.

As another theme in common with other subjects of this autobiographical series, one cannot miss the fact that Lemieux was a superb teacher. Choosing just one of his former students as an example - the extraordinarily gifted and charismatic Bert Fraser-Reid - one can see how much motivation and excitement has passed from teacher to pupil, qualities that are apparent to the audience each and every time Fraser-Reid presents his own world-class carbohydrate research results. By the many other gifted scientists that have graduated from his research guidance, Lemieux has left his mark on the development of academic organic chemistry. Of similar importance, it must also be pointed out that, just as he was willing to help academic institutions, Lemieux has also been involved throughout his career in industrial collaborative transfer of chemical technology. This constitutes an activity that surely has brought significant wealth and exciting employment opportunities to Canadian society. As a complement to the combination of brilliance, toughness and persistence, Lemieux also has an admirable reputation within the scientific community as a person of the highest ethics and decency.

His legendary honesty paid handsome dividends when he was given a generous co-authorship by the late W. S. Johnson in recognition of his independent contributions to the development of both the periodate-permanganate and the periodate-osmium tetroxide oxidative reagents for the cleavage of olefins.

In closing, one of the most interesting aspects of these autobiographies is that they provide a forum in which members of our profession with uncommon levels of wisdom can comment on the state of science and its future. Lemieux is no exception. One of his most intriguing monologs appears in pp. 3-4. As part of a general commentary on funding practices of science, Lemieux raises issues that go to the very value foundations of late twentieth century science. He argues his sense that a career in science must transcend finding timely topics with high prospects of funding and publication. Instead, he believes that working in science is far more than just a way to earn a living. Rather it is a commitment to the joy of discovery that requires the most dedicated of individuals. When one looks about at the perplexing state of the U.S. science and engineering professions of the 1990's with their recurrent problems of industrial downsizing, limited academic opportunities, underemployment, and chronic sub-funding,

one can't fail to notice that Lemieux may be on to something. Has there been too much of an emphasis on vocational training in science and engineering over the past few decades? At the obvious risk of oversimplifying, nevertheless, we are all aware that the excitement of excellence and spirited inquiry still held high by the faithful few are at risk of being displaced by faculty viewing careerism as more important than teaching, by minimalist students cynically seeking "dream jobs" simultaneously combining salary, security, and leisure, and by industrialists more concerned with quick fix/bottom line concerns than putting out the very best product. This was not and could not be right. It is left for certain special individuals to teach by the very examples that their lives provide and, in so doing, to permit the rest of us at least to glimpse how it should be. The saga of their lives unequivocally illustrate a pathway to the highest standards of professional dedication and to the internal rewards that can come with such a commitment. The rest of us may have quite a way to go but no excuse for not having at least been shown the path by scientists such as Lemieux.

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Lavoisier in European Context: Negotiating a New Language for Chemistry. Bernadette Bensaude-Vincent and Ferdinando Abbri, Editors, Science History Publications/USA, Watson Publishing International, Canton, MA, 1995, x + 303 pp. Cloth (typeset), ISBN 0-88135-189-X.

Sometimes a well-researched historical event or period, especially one in our own field, is so familiar that the story seems complete. Then a new book appears, one that provides the unexpected illumination and may even awaken our dozing imagination about the fruitfulness of still further revisiting. Such a book is this collection of fifteen essays about the spread of the new, French chemical nomenclature associated with Lavoisier and the chemical revolution at the end of the

eighteenth century. The book is based on a historiographic workshop organized under the auspices of the European Science Foundation as a complement to the cultural events celebrating Lavoisier's Bicentennial in 1994. Twelve of the essays are in English, three in French. The length of each varies from eight to thirty-six pages, the median length being eighteen pages. The book also includes a thirteen-page, briefly annotated bibliography on the two landmark French volumes *Méthode* and *Traité* and their European translations (1787-1800).

Each essay is written by a different author, including the two editors. The introductory essay, by one of the editors, provides an overview of the context, and the final one gives a summation and concluding remarks. The thirteen essays in between describe "the diffusion of the new nomenclature designed by four French chem-

ists—Louis-Bernard Guyton de Morveau, Antoine-Laurent Lavoisier, Claude-Louis Bertholet, and Antoine-Francois de Fourcroy—all over Europe.” Each essay focuses on a single country: Sweden, Belgium, Poland, Netherlands, Scotland, England (two essays), Portugal, Spain, New Spain (Mexico), France, and Italy (two essays). Notably missing is an essay on Germany, “due to the last moment cancellation of one participant.” Most of these countries are often omitted from accounts about the chemical revolution, and, as one of the authors puts it, this view from the fringe teaches us something about the development of chemistry as a whole at the end of the eighteenth century.

The spread of the new, French chemistry, we read in the introductory essay, helped chemists achieve a sense of belonging to a coherent discipline. The essays examine that spread as it was influenced by national cultural differences or at least the attitudes of some influential chemists that determined each national response. The thrust of all the essays is conveyed by a statement in one of them: “To say that Dutch chemists converted to the ‘new’ chemistry says little if we do not explore what sort of filter their commitments and practices provided for the reception of novelties and what shape those novelties took as they were integrated into the Dutch field.” The names and contributions of several of the cast members on stage in these essays are likely to be familiar only to chemists in the same country, at most. But contributions they did make. “The new language was neither accepted nor refused, but rather debated and negotiated. European chemists rarely showed a passive attitude of simply being ‘receivers’.”

Part of the debate and negotiation—a substantial part, in fact, this book makes clear—was about the new language itself. That is, for example, not only about the role of oxygen in combustion but also about the name oxygen (=acid former) for that substance. “The new language was deeply theory-laden,” and Davy, among others, favored a theory-free language. (For example, his “chlorine” did not imply either element or compound, a matter of some uncertainty at the time.) One assessment of the major effect of some of the new systematic names was “irreparable injury to science.” Subdued echoes of that attitude can be heard even now from some quarters in response to efforts by the nomenclature commissions of IUPAC to make chemical nomenclature increasingly *tic*. Forsaking the familiar, especially language, is difficult to do. Chemists often seem to grasp and acknowledge improvements in chemical theories more easily than in chemical nomenclature. This book identifies the different kinds and degrees of resistance

to the new, French language of chemistry two centuries ago, country by country, and highlights individual chemists contributing to the outcome of the debate. As *la gniappe* (a south Louisiana term for a pleasing extra), this book provides a capsule history of higher education in Portugal.

Because the book is about language, I had not expected it to be annoyingly inconsistent in its treatment of language; but it is. Most of the twelve English-language essays include numerous quotations from the original, non-English language. One author gives only the English translation, with reference citation to the original Dutch. Some others use the original in the text and provide translations in end-of-the-chapter notes. (The reverse placement—English in the text, original in the notes—would have been far more convenient for the reader without any loss of accuracy or authenticity.) Others translate a quotation of a few words in the text and quickly use a longer one, without translation anywhere, to extend or contrast the point made by the first. In the essay that strongly emphasizes the dominating influence of an estimable translation on the reception of the French proposals in Italy, no translations of the French or Italian passages are provided. Some of the significant points being made by the authors are likely to be missed by many American readers, even older ones who had to pass language examinations as part of their Ph.D. degree requirements.

Even so, the major points will not be missed. The centrality of contentions about nomenclature in the chemical revolution at the end of the eighteenth century will probably be a new viewpoint for many readers. The revolution is presented not as the indomitable triumph of cold, passionless reason set forth by one person, not as “exclusively a French-English *affaire*.” It is, instead, treated as broadly international, dependent on numerous unacclaimed chemists who interacted with passion stemming from a variety of institutional positions, social prestige, and attitudes. Such personal perspectives of the chemists in the development of chemistry are always important but often unacknowledged. Those highlighted in this book are perspectives on authority and liberty, on collegiality and disciplinary boundaries, on empiricism and theorizing, on innovation, on complexity of instrumentation and its effect on lay (audience) participation in scientific experimentation. The diverse humanity of the chemists dominates the story—as it must have dominated the event. *James G. Traynham, Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803-1804.*