

RETIREMENT

Honoring Professor Asher Mandelbaum

The purpose of this column is to honor Asher Mandelbaum, Professor Emeritus at the Technion-Israel Institute of Technology, Haifa, Israel, following his retirement, and in recognition of his important and enduring contributions to the elucidation of mass spectral stereochemical effects of organic gas-phase ions. As one of Professor Mandelbaum's many fortunate students, I am proud to describe here a selected few of his professional achievements, apologizing that the presentation cannot do justice to either the elegance of his experiments' design, or the depth of wisdom and insights underlying his interpretation of the results.

To give Professor Mandelbaum's work some historical perspective, this year marks the 100th anniversary of the field of mass spectrometry, which has significantly evolved over the past century. Most of those who use today's sophisticated computerized mass spectrometers, equipped with various ionization techniques, consider mass spectrometry to be predominantly an analytical tool. This view has become particularly widespread over the last 20 years since the first instruments with electrospray ionization became commercially available, thereby enabling the routine analysis of non-volatile compounds. Prior to that turning point, however, a large proportion of contributions to the field focused on the use of mass spectrometry to obtain insights into the fundamental chemistry of gas-phase ions. Notably, it was in the 1950s that Beynon, McLafferty, Meyerson, Ryhage, Stenhagen, and others found that structural information could be gleaned from the MS fragmentation of organic compounds containing various functional groups. The following decade became the budding period of organic mass spectrometry, with advances by other research teams, including those of Biemann, Budzikiewicz, Djerassi, Spiteller, and Williams, and with the publication (1968) of the first mass spectrometry-dedicated journal, *Organic Mass Spectrometry*.

During that time, in the early stages of his academic career, Professor Mandelbaum became interested in studying the cause of the different fragmentation behavior of configurational and conformational stereoisomers in many organic systems. Around 1965, he had the opportunity to measure the mass spectra of stereo-isomeric morphine derivatives from the collection of the late Professor David Ginsburg, then Dean of



the Technion's Chemistry Department. The mass spectra reflected entirely different behavior of the stereo-isomers, results that could be elegantly explained by mechanistic arguments. It was clear that the high stereo-specificity of certain fragmentation processes indicated retention of structures of the parent ions, despite only a small difference in the energies of the stereo-isomers.

In the following years, Professor Mandelbaum's research group investigated the mass spectra of stereo-isomeric pairs from a wide spectrum of organic systems, and proposed mechanisms for the stereo-specific processes. For instance, a variety of mono- and polycyclic cyclohexene derivatives were shown to undergo a highly stereospecific retro-Diels Alder (RDA) reaction, but in only one isomer. This finding led to the conclusion that the two bonds involved in the RDA fragmentation of gas-phase ions are cleaved concurrently. That conclusion, in turn, suggested a concerted mechanism for the gas-phase cycloreversion process, analogous to the accepted

mechanism of the RDA reaction for neutral cyclohexenes in their ground electronic state. Another set of studies dealt with the highly stereospecific RDA fragmentation accompanied by a two-hydrogen migration for some polycyclic diones, and its dependency on the size of certain rings in the system. The results were interpreted in terms of a conformational effect on the distance between the H-atoms and the carbonylic oxygen atoms.

Professor Mandelbaum's lab provided many examples in which a "hidden hydrogen transfer" step preceded the specific or stereospecific elimination of alkyl radicals, alcohols, and halogen atoms. One such case studied a cyclic and an acyclic system in which mass spectrometry was shown to be an effective tool for the determination of configuration, which is difficult to achieve by other spectroscopic techniques. Other topics explored in his lab over the years included: configurational and conformational effects on intramolecular proton transfers upon chemical ionization (CI) and collision-induced dissociation (CID) conditions; internal hydrogen bonding under CI; the effect of steric hindrance on gas-phase protonation and on subsequent fragmentation behavior; and the role of anchimeric assistance in fragmentation under CI and CID conditions. In summary, the various studies undertaken in Professor Mandelbaum's lab are valuable not only for their inherent academic interest, but have also led to mechanistic interpretations that are of diagnostic importance for differentiating the isomers in the systems investigated.

Over the course of his career, Professor Mandelbaum wrote several significant reviews. Most were dedicated to discussing how stereochemistry influences the mass spectral fragmentation process. They offer useful, in-depth discussions of how thermochemical and kinetic considerations can explain differences in the mass spectral behavior of

stereoisomers. The clear presentation of the material and the provided examples that have become classics are as valid and relevant today as when originally written. Another contribution that Professor Mandelbaum conveyed through a review paper involves the "even-electron rule." By compiling evidence from a large number of organic compounds that violate the rule, he convincingly argued that it cannot be considered a "basic principle" in mass spectrometry and that even the term "rule" should be deemed unjustified.

Professor Mandelbaum is recognized by his peers as one of the preeminent representatives of his field, yet remains a man of rare modesty. He has given invited keynote lectures at international mass spectrometry conferences and collaborated with many colleagues abroad in France, Germany, Italy, The Netherlands, Switzerland, the United Kingdom, and the United States. At the Technion, he served as a highly-appreciated classroom professor, as Dean of the Chemistry Department, and as an advisor of many M.Sc. and D.Sc. students within his own lab. His support and encouragement of students, consistently provided in a forthright but gentle-mannered fashion that fosters their independence, growth, and self-confidence, are a hallmark not only of his integrity and expertise as a teacher, but of his characteristic treatment of every individual with respect. In turn, Professor Mandelbaum has earned the respect and admiration of all of us whose lives have been enriched by a personal and/or professional relationship with him. We wish him continued good health and fulfillment in his retirement.

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