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EDITORIAL

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# How I have learnt to ignore bibliometrics

In 1970, when I started doing research in physical organic chemistry as an undergraduate at the Natural Sciences Faculty of Charles University in Prague, the various forms of bibliometrics, such as impact factors, citation indexes, and the h-factor, were unknown. In those days, the quality of research was judged by its novelty, elegance, and usefulness, which in turn was discussed with colleagues and appreciated after one read the papers or attended a lecture. Things have changed since, and now many an academic or government bureaucrat is collecting bibliometric information on scientists in their institution and journals they publish in, to perform what is essentially a scalar ranking similar to a body mass index (BMI). This situation has been eloquently criticized by Molinie and Bodenhausen (Molinie & Bodenhausen, 2010) and wholeheartedly endorsed in an essay by Ernst (2010). The former authors then proposed a different index, named tongue-in-cheek the *k*-factor, where *k* stood for kinship (Molinie & Bodenhausen, 2011). It is illustrative that according to SciFinder, the Molinie–Bodenhausen papers have collectively been cited four times since publication. The obvious problem with the various indexes is that they do not relate the bibliometric response to the paper's scientific quality or usefulness. To highlight the point using examples from my own production, let me take my most frequently cited article (thinly veiled here as paper 1, >6400 citations since 1999) and compare it with my other paper (paper 2) with about 108 citations since 1984. According to these figures, paper 1 should be 59-fold better. However, when I use a different metric, such as how frequently these papers are read, the ratio is reversed, as the 1984 paper has been receiving, on average about 1000 reads annually over the last several years, while the 1999 paper is not read much. This raises two questions: (1): Would you not prefer having your papers widely read rather than cited? and (2): if people don't read an article, what is the point of citing it? With this in mind, I am taking the opportunity in this essay to reminisce on a few past research projects that were reported in papers that I value despite their abysmally low citation count.

## 1 | CASE 1: RETRO-DIELS ALDER REACTION IN CATION RADICALS

This project was inspired by a short communication (Smith & Thornton, 1967) that the retro-Diels Alder reaction (RDA) of ionized 4-vinylcyclohexene produced the charged butadiene fragment ions at an unequal ratio, depending on whether they originated from the ring or side-chain of the precursor ion. This dissociation is formally analogous to the retrogression of the well-known Diels–Alder reaction of 1,3-butadiene, which can be promoted thermally in the gas phase. Charge distribution between fragments arising from a singly charged cation radical is a very sensitive function of the ionization energies of their neutral counterparts, according to the Stevenson-Audier rule (McLafferty & Tureček, 1993). In the case of 4-vinylcyclohexene, the fragments formed from the diene (ring) and ene (side chain) parts should be 1,3-butadiene. To test the interpretation of this very unusual and unique phenomenon, we decided to study the RDA of 4-vinylcyclohexene that was complementarily labeled with deuterium in the ring and side-chain parts of the molecule and compare the results with those of Smith and Thornton. In addition, we made complementarily labeled limonene (isoprene dimer), as well as deuterium-labeled bicyclic dimers of 1,3-cyclopentadiene and 1,3-cyclohexadiene (Tureček & Hanuš, 1980). The idea was to compare RDA in systems, such as 4-vinylcyclohexene and limonene, in which the side-chain becoming the ene-fragment could rotate and assume different rotamers, as opposed to the other tricyclic dimers where both the ene and diene parts were fixed in rings. The results showed that RDA of 4-vinylcyclohexene and limonene ions favored the formation of the side-chain ions by about 15% with only a weak dependence on the ionizing electron energy. The cyclopentadiene and cyclohexadiene ions were formed more or less symmetrically (±4%) from both parts of the dimer precursor ions. We concluded that the conformation of the side chain affected the energy of the incipient diene fragment, favoring its ionization. Nevertheless, this explanation was riding on the assumption that RDA was a single-step concerted dissociation, a topic of much interest in the

1970s. It took a few years to engage the help of a theoretician colleague to address this question in a more profound and physically relevant fashion. To do that, we used the Topological Molecular Orbital theory developed by Jiří Pancíř (Pancíř, 1982) and mapped the entire potential energy surface for RDA in the ground and the first excited electronic state of the 4-vinylcyclohexene cation radical, including all conrotatory and disrotatory modes of bond dissociation, intermediates, and transition states (Pancíř & Tureček, 1984). To our surprise, the dissociation in the ground electronic state of the cation radical clearly preferred a stepwise mechanism that was triggered by the cleavage of the doubly allylic C5–C6 ring bond forming an intermediate. The parts of the potential energy surface corresponding to the supra-supra or supra-antara concerted ring cleavage modes were energy maxima and therefore were dynamically excluded according to the Murrel–Laidler rules (Murrell & Laidler, 1968). However, in the open-ring intermediate, which was a local energy minimum, the former endo (ring) and exo (side chain) groups were identical, so there was no reason why they should differ in sharing or giving up the electron and becoming butadiene neutral molecules or ions. In contrast, RDA in the first excited electronic state of the 4-vinylcyclohexene ion showed a saddle point for the supra-supra concerted process. In addition to explaining a bizarre charge distribution phenomenon, these 1984 calculations showed a remarkable agreement with experimental ion energies obtained by threshold energy measurements and photoelectron spectroscopy. The seldom cited 1984 paper was one of the first if not the first combined experimental and computational study of the potential energy hypersurface of a polyatomic gas-phase cation radical in multiple electronic states.

## 2 | CASE 2: FEMTOSECOND ELECTRON TRANSFER AND FAST KINETICS OF TRANSIENT RADICALS

When I moved to the University of Washington in 1990, I started building an instrument for the production and study of transient neutral molecules and radicals using femtosecond electron transfer. Collisional electron transfer at high (keV) ion kinetic energies was the basis of neutralization-ionization mass spectrometry (Danis et al., 1983), for which we were building a tandem mass spectrometer of a new type (Tureček et al., 1992). The instrument consisted of two quadrupole mass analyzers separated by an acceleration-deceleration lens system including two collision cells, one for neutralizing and the other for reionizing collisions. The collision cells were spaced by 60 cm and were floated at high negative voltages to handle cations. Ions produced by collisional reionization were decelerated and filtered by kinetic energy in an asymmetric chicane lens before mass analysis by the second quadrupole. The vacuum regions housing the acceleration and deceleration components were separated by a gate valve maintained at the ground potential, creating an inadvertent focusing einzel lens. The 60 cm total length of the fast neutral path in this instrument inspired the idea of utilizing this region for kinetic measurements of neutral and ion dissociations on the microsecond time scale. To accomplish that, we inserted a segmented tubular lens consisting of four pieces that could be independently floated at a high deceleration and low stopping potential. The segment was used as a reionization collision cell, but depending on the applied potential pattern, we were able to monitor neutral dissociations occurring in the region that was maintained at the stopping potential and separate them from ion dissociations taking place in the region maintained at the high deceleration potential. Since the ion and neutral velocities were known accurately, it was simple to define the time scale for the dissociations by the length of the pertinent segment and derive unimolecular dissociation rate constants from the measured dissociation rates (Kuhns & Tureček, 1994). The instrument and variable kinetic method described in this rarely cited paper has been used over the years to establish the dissociation kinetics of numerous transient molecules and radicals relevant to atmospheric chemistry, combustion, and high-energy chemistry.

## 3 | CASE 3: PREPARATIVE SEPARATION OF MIXTURES BY MASS SPECTROMETRY

1998 was a great financial year for the pharma industry, and some companies with extra cash were looking for collaborations with academic research labs. I was approached by Selectide, Inc., a drug development company in Tucson, AZ, about a project using mass spectrometry for the physical separation of drug candidates synthesized by combinatorial chemistry methods. The problems they faced with sub-nanomole quantities of their drug candidates were twofold. One was false positives, where an unknown contaminant would display activity that would not be reproduced when an authentic compound was synthesized in an appropriately larger amount and purified. The other problem was false negatives, where a contaminant would kill the assay leading to no results at all. The Selectide team wanted an

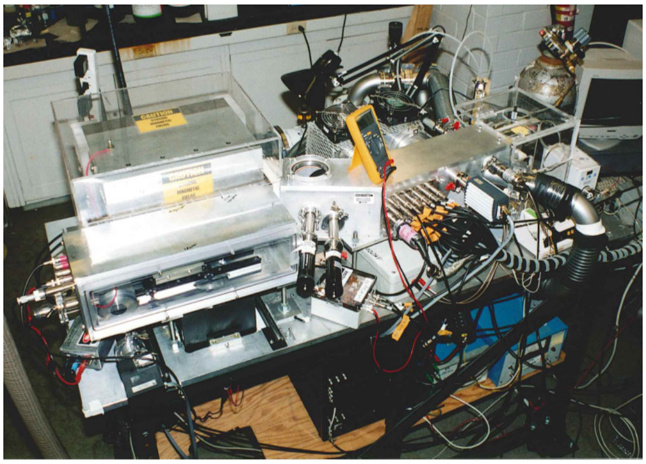

**FIGURE 1** Top view of the preparative mass spectrometer. Electrospray ion source on the right, permanent magnet, and ion collector on the left. [Color figure can be viewed at wileyonlinelibrary.com]

instrument to purify the small amounts stripped from beads, so their activity could be tested. Although preparative separation of uranium isotopes in the calutron had been known from the Manhattan project (Yergey & Yergey, 1997), the Selectide project unconditionally required that the compounds to be separated not be damaged upon ionization, ion neutralization, and isolation, which posed a number of challenges. To execute the project, I hired Adi Scheidemann and Terry Olney as post-doctoral research associates, and we designed and built a tandem mass spectrometer that was funded by Selectide. The instrument (Figure 1) was a Mattauch-Herzog type of an electric-magnetic sector that was equipped with an electrospray ion source for nondestructive ionization. The ion source and transfer optics were maintained at low potentials, and ion transmission was improved by a home-built ion funnel lens designed by Terry Olney. The source achieved hefty ion currents of 10–15 nA as measured after the ion funnel. Ions were then accelerated to 2 keV, energy dispersed by an electrostatic sector, and refocused on a 38-cm long focal plane by a large magnet. Since the magnet had to be floated at the acceleration potential, we opted for a large 1.6 T permanent magnet that was custom-built and insulated from the other parts of the instrument, as shown in the figure of a top view of the instrument with the 2-kV floated permanent magnet in a protective plexiglass case with a warning label. The multichannel ion collector is at the forefront. To achieve linear mass dispersion, the magnet was designed and built with curved poles where the decreasing magnetic field along the focal plane compensated the square root dependence of the ion trajectory radius on the ion $m/z$. During the 2 years of the instrument design and construction, the funding company went through several hostile takeovers, being gradually acquired by larger and larger international drug companies, eventually ending as a Sanofi lab. Fortunately, we succeeded in purchasing upfront all expensive parts, including the $100,000 magnet, so we could continue the work even when the company's new leadership largely lost interest in it. The magnet design had one flaw, which was that the ion exit trajectories were at relatively sharp angles with respect to the edge of the magnet poles, and the angles were sensitive to the ballistic angle of ion entrance into the magnet. This made it difficult to intercept the ion exit trajectories by a multichannel deceleration lens, so the mass-separated ions could be decelerated to low kinetic energies allowing soft-landing on the collectors. The problem was solved by Hak-No Lee, another postdoctoral associate working on the project. Hak-No used a high transmission grid to accelerate the ions exiting from the magnet from 2 to 7 keV while simultaneously bending their trajectories so they could be directed to a multichannel deceleration lens. After deceleration, the low-energy ions were soft-landed on a collector array which was maintained at a low potential to control the ion kinetic energy in landing. Nondestructive ion discharge in soft landing was achieved by treating the collector stainless steel surface to develop a thin layer of metal oxides that mediated nondestructive ion discharge by a coupled proton-electron transfer. Unfortunately, the shifting of company ownership and leadership had another adverse effect: it substantially delayed the publication of the first paper (Mayer et al., 2005). In the meantime, preparative ion mass spectrometry was published by another group. Although their instrument was a single-channel device and the ion landing was messy, they got the credit. Nevertheless, we retained a treasure chest of high-quality equipment that was then used for other projects on soft and reactive landing and spectroscopic characterization of surfaces and landed biomolecules.

## 4 | CASE 4: THE EARLY LIFE OF A PEPTIDE CATION RADICAL IN THE FIRST 330 FS

Electron capture (Zubarev et al., 1998) and electron transfer dissociation (Syka et al., 2004) of multiply charged biomolecular ions were exciting new methods for peptide and protein sequencing that almost immediately raised questions of the reaction mechanism and internal energy redistribution in the cation radical intermediates. It is not my intention to revisit the debate here, it has been covered in detail in another review

(Tureček & Julian, 2013). One puzzling aspect of these electron transfer phenomena was the possibility of the formation of different electronic states in the peptide cation radicals and their effect on ion dissociations. All evidence up to the point had been indirect and there were no experiments addressing the question. Fortunately, my graduate student Chris Moss who has been trained in molecular dynamics set out to use Ehrenfest ab initio dynamics to analyze time-development processes in a small peptide cation radical. We had experimental results for electron transfer to a doubly charged Ala-Arg peptide ion that were obtained by Steen Brøndsted Nielsen and his team at Aarhus University (Jensen et al., 2010; Panja et al., 2008). Those data were particularly valuable because the spectra were obtained by electron transfer from thermal cesium atoms to fast 100 keV peptide ions, and so the dissociations were monitored on the time scale of a few microseconds. Ehrenfest dynamics and the program for calculations had been developed by my colleague Xiaosong Li (Isborn et al., 2007; Li et al., 2005). It uses density functional theory to propagate electron density in 0.2 fs steps along the nuclear trajectory, starting from a selected electronic state. The calculations of each 330 fs trajectory for this open-electronic shell system ran for several weeks and were a virtual cliffhanger, because a computer crash would have meant a fresh start from the beginning. The results were quite revealing. Electron transfer forming the ground electronic state of the $(\text{AlaArg} + 2\text{H})^{+\bullet}$ cation radical triggered a fast competitive loss of ammonia from the N-terminus and cleavage of the N–$C_\alpha$ bond, which were the experimentally observed dissociations. Remarkably, the branching ratio for these dissociations was shown to depend on the initial ion thermal energy. Loss of a hydrogen atom, which was another experimentally observed dissociation, did not stand a chance to occur competitively on the ground electronic state. In contrast, it became the dominant and extremely fast dissociation starting from the third excited state of the cation radical where it involved one of the arginine hydrogens (Moss et al., 2012).

To summarize, I believe the above-described projects were fundamentally innovative, intellectually challenging, and fun to pursue. In my mind, this utterly overrides the low citation count of the papers they were reported in and makes me gladly thumb my nose at “the follies of citation indexes and academic ranking lists” to quote Richard Ernst.

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František Tureček

*Department of Chemistry,*
*University of Washington, Seattle, Washington, USA*

**Correspondence**
František Tureček, Department of Chemistry,
University of Washington, Seattle, WA 98195-1700, USA.
Email: turecek@chem.washington.edu

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