Theor Chem Account (2008) 119:1–3
DOI 10.1007/s00214-007-0287-5

INTRODUCTION

A Festschrift in Honor of Philip J. Stephens' 65th Birthday

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Received: 17 March 2007 / Accepted: 19 March 2007 / Published online: 4 May 2007

On the 9th of October 1940, under the blitz, John Lennon was born. On the exact same day, elsewhere in England, Philip J. Stephens came into this life. While the former was exploring strawberry fields, the latter was discovering new things about magnetic fields, and launching a scientific career that has had, and will continue to have, significant and enduring impact.

Upon the occasion of Professor Stephens' 65th birthday, the two of us, who are alumni of his group (GMJ 1994 and KJJ 1989), were inspired to assemble and co-guest-edit this special issue of *Theoretical Chemistry Accounts* ("TCA"). For this opportunity we are very grateful to Professor Christopher J. Cramer (Editor of TCA) and to Ingrid Samide at Springer, Heidelberg. Professor Stephens (Figs. 1, 2, 3) has provided us in this issue with *A Scientific Memoir* ("*Memoir*"), and we will not seek to repeat that here. Instead, we offer a few reflections from our own aggregate period with him (∼1980–1994), and a general introduction to the issue. Where papers are cited, they are from the references list in the *Memoir*.

Professor Stephens' contributions to molecular spectroscopy are fundamental and span both theoretical and experimental aspects and applications ranging from organic to bioinorganic chemistry. No other individual has contributed more to pioneering the fields of magnetic circular dichroism (MCD) and vibrational circular dichroism (VCD).

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Professor Stephens' theoretical formalism of MCD remains the foundation upon which the field was built, and his personal efforts in developing instrumentation and in marrying experimental and theoretical aspects in a diverse set of fields proved the significance of MCD as a tool in the study of electronic spectra, from the vacuum ultraviolet to the near infrared (IR). Especially fruitful applications were found in the study of transition metal systems and metalloproteins (including *inter alia* heme, copper, and iron-sulfur proteins).

The experimental breakthroughs in near IR CD and MCD led to a drive to measure VCD, across the IR, and with this successfully accomplished, a theoretical foundation for VCD was developed in order to predict spectra. This latter included the breakthrough determination of methods for the calculation of magnetic dipole transition moments. Stephens' work continues to lead to ever wider utilization of VCD and, more recently, optical rotation, to solve stereochemical problems in Nature, the organic laboratory, and in pharmacology, all of which are dominated by chiral molecules. Again, Professor Stephens' *Memoir* is the best place to navigate this wonderful journey.

As with most significant scientific achievements, in addition to the forward progress directly sought and described above, there are ripples of impact that were unanticipated in the original set of objectives, and some of these have on their own proved quite significant. We provide herein just a few examples, biased by our time at USC.

The CD and MCD work on metalloproteins led to a project involving *Azotobacter vinelandii* Ferredoxin I (AvFdI), an iron-sulfur protein then thought to be important in nitrogen fixation. As described in the *Memoir,* this protein contains both 4Fe and 3Fe iron–sulfur clusters, the latter species being novel at that time. A spectroscopic study of this protein, built on the backbone of CD and MCD spectroscopic data, concluded that the published X-ray crystal structure must be in

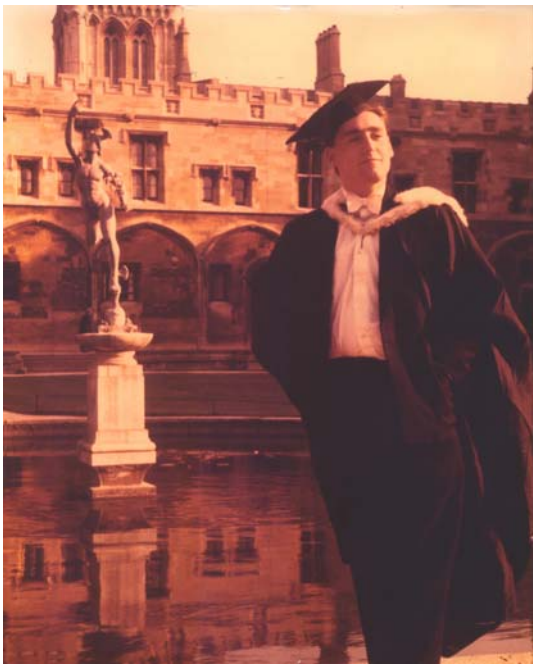

Fig. 1 A 1962 picture on the day Philip Stephens received his BA degree from Oxford: taken in the main quad of his college, Christ Church

Fig. 3 A recent picture of Anne-Marie and Philip J. Stephens

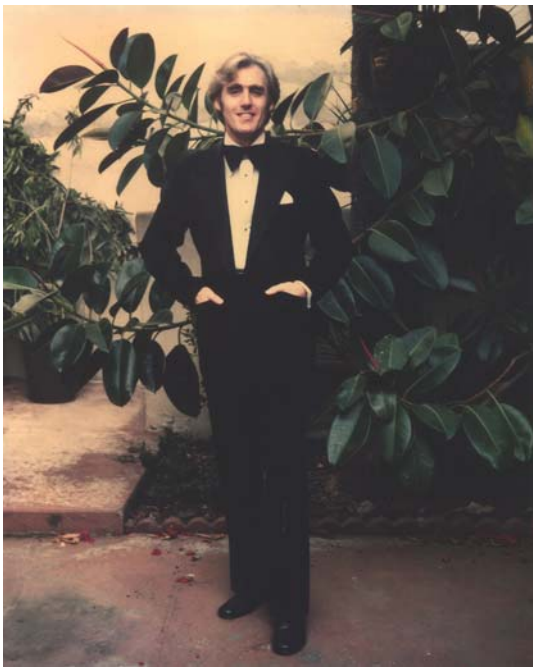

Fig. 2 A 1977 picture on the day Professor Stephens received the USC Associates Award for Creative Scholarship and Research (a black-tie affair)

error (*Memoir* reference 77). One of us, on presenting this paper at a group meeting while still at UCLA, was told half-seriously by a now famous crystallographer that the structure was "too pretty to be wrong". Indeed, this structure was incorrect. Re-determination of this structure was obviously a boon to AvFdI and to understanding iron-sulfur proteins more generally, but beyond this, in the immediate wake of these discoveries, a number of other, more famous protein structures were also shown to be incorrect, all published in the late 1980s from high profile laboratories. This in turn has led to substantial improvements in crystallographic methods especially in the recognition of bias in structure refinement algorithms.

Directly from site-directed mutagenesis experiments designed to address the correctness of the AvFdI crystal structure was the first demonstration of a process of new ligand recruitment by protein metal centers in response to mutagenesis (*Memoir* reference 111). This is a phenomenon that has been noted repeatedly since then and has become a standard aspect of protein sequence alignment exercises.

Another site-directed mutagenesis experiment designed directly to address protonation of the reduced AvFdI 3Fe center, which phenomenon was seen and characterized by MCD work (*Memoir* 115), then led to the elucidation of a novel electron transfer mechanism for AvFdI and potentially for many other similar proteins (*Memoir* 128).

One can also easily find such examples from the VCD work. The quality of the predictions of VCD spectra by Stephens' procedures proved to be very sensitive to the quality of the participating force field. Interrogation of force field quality by the corresponding quality of VCD predictions led to early demonstration of the value of hybrid density functional theory methods e.g. as compared to more expensive MP2 methods. *Memoir* references 132 and 136 have been

cited well over 1,000 times in this context, a large fraction of which citing publications have no relationship to VCD.

More directly, the creation of Stephens' equations for VCD and the implementation of the new and fundamental tensor determinations in readily available software programs has enabled work in microwave spectroscopy, Raman optical activity, optical rotation, and magnetic susceptibilities to be developed and carried out.

As noted above, these are but a few examples.

In addition to his research at USC, Professor Stephens brought to USC the high quality of teaching from Oxford, where the famous tutorials and small lectures are renowned for turning out highly trained and educated students. While many academics neglect their teaching because it does not carry the prestige of research, Professor Stephens has brought a high standard of teaching to USC and passed it on to his PhD students, many of whom won teaching awards while giving tutorials in physical, analytical, theoretical and general chemistry. The next generation of researchers and academics who have had the fortune of attending one of Philip's lectures have taken something away with them. In more than one case, he would teach a whole course to a single interested student. In addition, he always has had an open door policy with respect to answering questions in theoretical, physical, inorganic, and biochemistry, many times being able to answer questions which were not able to be answered by anybody else, including those responsible for teaching the relevant course. His ability and willingness to pass on his wealth of knowledge and understanding to both undergraduate and graduate students, as well as postdocs and visiting academics, has been a great example to all who worked with him.

Turning to this TCA festschrift, we are grateful for a diverse and excellent set of papers to honor Professor Stephens. Professor Stephens himself has provided a state of the art example of determination of absolute configuration by VCD using the methods he developed. McDowell and Professor A.D. Buckingham explore theoretical treatments of red- and blue-shifted proton magnetic resonances in linear hydrogen-bonded complexes. Professor Harry Gray's group has provided a theoretical study of the electronic structures of tetragonal nitrido and nitrosyl metal complexes, with emphasis on comparing their inner coordinate electronic structures. Professor Laurence A. Nafie provides an exposition of near resonance theory for Raman scattering and Raman optical activity. Gorelsky and Solomon provide a new molecular orbital method for investigation of electronic structure contributions to the redox properties of transition metal systems, with a focus on the contributions of electronic relaxation. Cao et al. provide progress in reduction of contaminating linear-birefringence in VCD measurements. Kim et al. report on efforts of the Keiderling laboratory in studying the sequence dependence of IR and VCD spectra for beta turns in proteins. Lazzeretti, Soncini, and Zanasi explore the utility of response tensors for chiral discrimination by NMR. Male et al. provide one of the two papers in the issue treating MCD, and provide application of a new integrated spectroelectrochemical system to cytochromes. Hug and Fedorovsky provide a novel method for simplifying comparisons of molecular motions of structurally similar moieties in otherwise different molecules. MacKenzie et al. provide a broad range of spectroscopic and analytical applications to antipodean geochemistry. Solheim et al. provide the first theoretical investigation of solvent effects on MCD B-terms using density functional theory. Nicu et al. introduce the implementation of the atomic axial tensors required for rotational strengths for VCD in the Slater-type orbital based Amsterdam Density Functional Package. Gould et al. provide novel new definitions of bond order, covalency, and ionicity of molecular bonds. From Curtin, we are honored to provide, along with our collaborators, a series of theoretical and experimental studies of phenyloxiranes (Fristrup et al.), L-Histidine (Deplazes et al.), Aframodial (Jalkanen et al.), L-Alanine (Jalkanen et al.), substituted cyclopropanes (Jalkanen et al.), and an application of knot theory to protein folding (Ramnarayan et. al.). Finally, from Gilead, a touch of spectroscopy plays a role in the development and analysis of lipid based propofol dispersions (Jensen et al.). In all, a fine collection of work which we hope is worthy of the honoree.

We are both profoundly grateful, both to Providence and to Professor Stephens, for giving us our own launching pad in science. USC chemistry at this time featured a thriving physical chemistry environment, still steeped in the presence of Professors Arthur Adamson and Sidney Benson, of which Professor Stephens' group was an integral part. This provided an ideal learning environment that has indelibly marked each of the students who went through it.

As a final note, we emphasize that this is but a snap-shot of a work in progress, and we wish Professor Stephens many more years of fruitful labor in the service of science, as well as all personal best wishes.