Bob Squires: “Reactive organic intermediates. Benzynes, trimethylenemethane and beyond”

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Hilkka Kenttämaa

Department of Chemistry, Purdue University, West Lafayette, IN 47907-1393, USA

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Introduction

This focus issue of the *Journal of the Chemical Society*, *Perkin Transactions 2*, honors the memory of Professor Robert R. Squires, whose love for chemistry almost exceeded his love for life. Bob’s research focused on the properties, structures and reactivity of organic and organometallic reactive intermediates. Some of the species he studied are illustrated in Scheme 1. Bob created an impressive amount of knowledge during his short life (1953–1998). He did not make compromises in his search for in-depth understanding of chemical phenomena. He did not select problems that would be easy to address but problems that needed to be addressed. He tackled them by bringing together elegant, carefully designed gas-phase experiments, sophisticated mass spectrometry instrumentation, and high-level molecular orbital calculations.

Bob grew up in California and graduated with BA from California State University at Chico. He received his PhD in 1980 from Yale where he studied steric effects under the supervision of Professor Ken Wiberg. He moved to Boulder, Colorado, for his postdoctoral education. There he carried out research with Professors Chuck DePuy and Veronica Bierbaum on gas-phase negative ion chemistry in the flowing afterglow apparatus. In 1981, he accepted a position as an Assistant Professor at Purdue University, where he was promoted to an Associate Professor in 1986 and a Professor in 1990.

Robert R. Squires

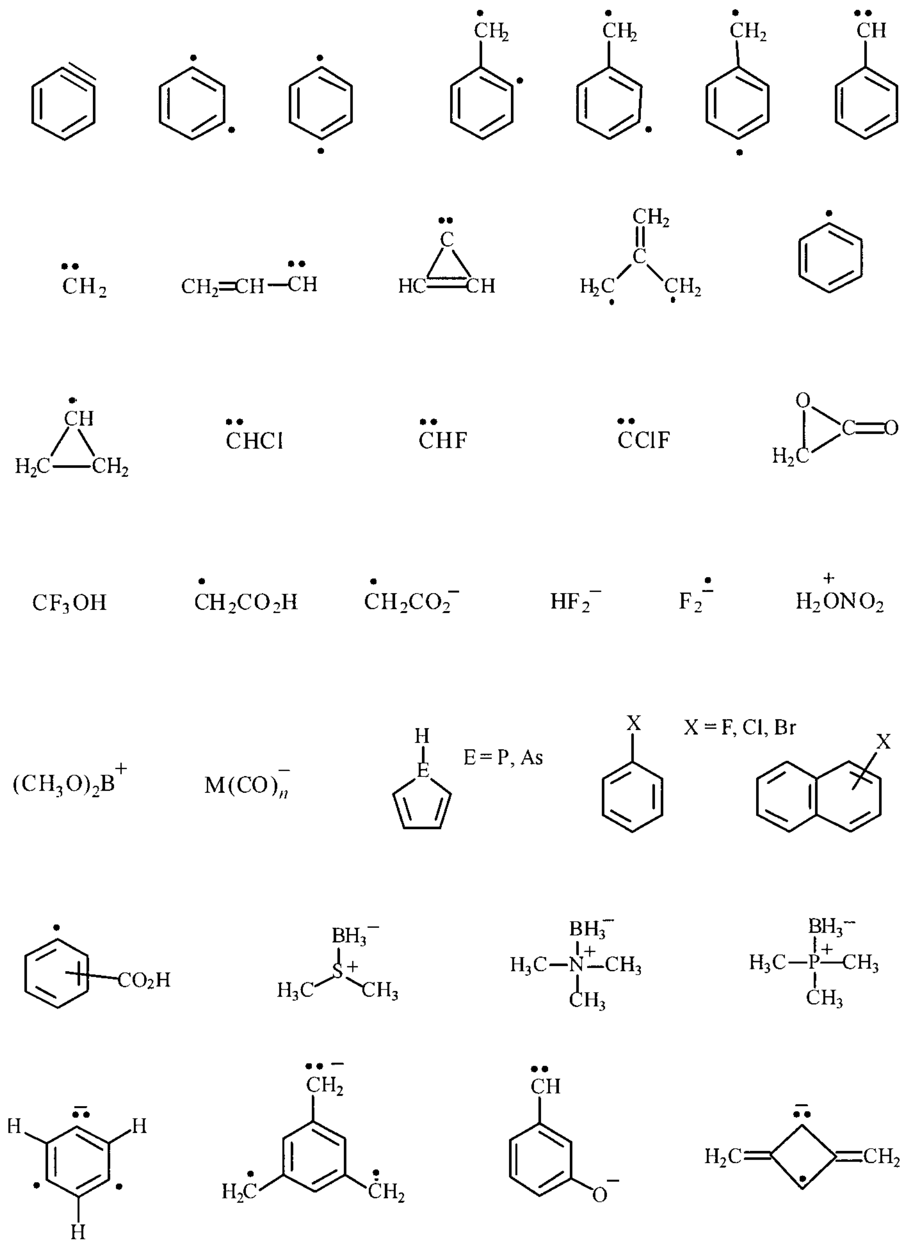
A glimpse into some of Bob’s most significant research accomplishments is provided below. The focus is on the work that Bob himself chose for his award address, “From Protein Folding to Carbene Chemistry: New Horizons for the Flowing Afterglow Technique”, given in June 1998 when he received the Biemann Medal of the American Society for Mass Spectrometry—just four months before his death. Statements that Bob made in his talk are included as an effort to illustrate his wonderful sense of humor.

Flowing afterglow technique: Mr Potato Head of mass spectrometry

Bob’s experimental gas-phase work was based on the use of the flowing afterglow technique.[1,2] This experimental method was developed nearly 40 years ago by Ferguson, Fehsenfeld and Schmeltekopf for studying ion/molecule reactions relevant to upper atmosphere chemistry.[3] The basic flowing afterglow instrument consists of an ion source, a room-temperature, relatively high-pressure (~0.5 torr) flowing-gas reactor, an ion sampling system, and a quadrupole mass analyzer. Multistep ion/molecule reactions are initiated by ion generation (usually by electron ionization). The reactions of these ions are studied by adding pure gaseous reagents through the inlets located along the tube. Either the positive or negative ions are sampled through a pinhole orifice into the low-pressure chamber for mass spectrometric analysis. The original instrument had a Pyrex flow tube and used a large-scale microwave discharge cavity for the ion source, such that one could easily see the visible afterglow (emission) from the excited species in the flowing plasma. It is from this phenomenon that the technique derives its rather poetic, “mantra-like” name.

A key characteristic of the flowing afterglow technique that accounts for its continued growth and broad applicability is the flexible, modular design of the basic instrumentation. This feature has enabled the creation of a host of useful new instrument configurations by mixing-and-matching different ion sources, flow reactors and analyzers (in the thirty or so flowing afterglow labs scattered throughout the world),[4–6] and it is the reason why Bob lovingly named the flowing afterglow technique as “Mr Potato Head of Mass Spectrometry”. Two of his most significant contributions to the evolution of the flowing afterglow technique involve the incorporation of a triple quadrupole-type tandem mass spectrometer, and bringing electrospray ionization into the world of flowing afterglow. These developments are discussed below.

Soon after building his first flowing afterglow apparatus at Purdue, Bob realized the vast possibilities that existed for a flowing afterglow apparatus equipped with a triple quadrupole mass analyzer. He demonstrated the viability of this instrumental configuration by temporarily constructing a prototype instrument that consisted of his flow reactor and an analyzer borrowed from one of Graham Cooks’ Finnigan instruments.[7] Soon afterwards, Bob built a flowing afterglow-



Scheme 1

triple quadrupole instrument (Fig. 1) that was to be the main work-horse in his laboratory for the following fifteen years.[6,8] The initial motivations for adding a triple quadrupole analyzer to the flowing afterglow instrument were two-fold: to permit analysis of the structures of ions produced in the flow reactor by collision-induced dissociation experiments, and to use the flowing afterglow as a chemically versatile ion source for MS/MS experiments. The instrument served admirably in both respects over the years. Bob and his students later added a fourth quadrupole between the ion source region and the front end of the flow tube, thus generating a selected-ion flow tube-triple quadrupole apparatus (SIFT-QQQ).[9] This device allows selection of the reactant ion that enters the flow reactor, and hence provides an opportunity for clean studies of ions formed as minor components in the ion source.

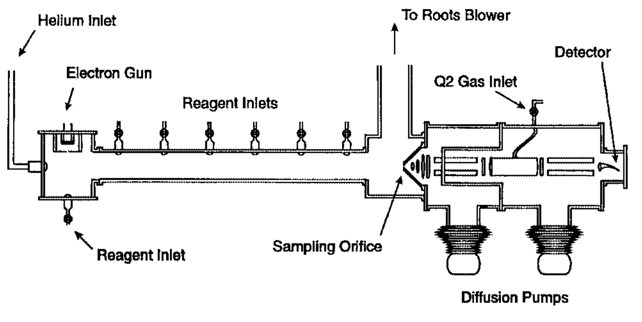


Fig. 1 The flowing afterglow-triple quadrupole apparatus constructed in Bob's lab.

With new instruments, the greatest challenge is to discover their unique capabilities, that is, to identify experimental modes of operation that make use of the individual components in a fully integrated fashion. The measurement of kinetics for isomeric and isobaric ion–molecule reactions, *i.e.*, reactions involving reactant and product ions of the same exact or nominal mass-to-charge ratio, respectively, is an example of such an application of the flowing afterglow-triple quadrupole instrument.[10] Normally, the kinetics of such reactions cannot be determined without isotope labeling. However, Bob and his students got around this problem by not monitoring the intensities of the actual reactant ions, but rather the intensities of their characteristic CID fragments, which were produced "on-the-fly" during the experiment. The measured depletion of these monitor ions was shown to provide a reliable means of determining the rate coefficient for the overall reaction taking place between the reagent ion and a neutral reagent in the flow

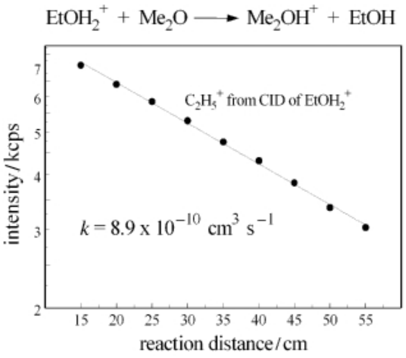


Fig. 2 Rate measurement for the proton transfer reaction between $EtOH_2^+$ and Me_2O. Note that the reactant and product ions are isomeric.

reactor. For the example shown in Fig. 2, this involved monitoring of $C_2H_5^+$ as an isomer-specific surrogate ion for the reactant ion that displays the kinetic decays necessary for obtaining the overall reaction rate coefficients.

Another major advance in instrumentation was the combination of electrospray ionization with the flowing afterglow method to give a techique that Bob and his students dubbed "flowing afterspray".[11] They demonstrated that ions can be electrosprayed from a high-voltage syringe needle directly into the flow tube through a foot long heated capillary, without the need for differential pumping or ion focusing. Detected ion currents as high as 3 pA were achieved, and the results obtained to date indicate little or no reclustering of the desolvated ions with the background solvent vapor in the flow tube. The capillaries can be located at different positions along the flow tube, which may allow the examination of ion–ion reactions through the use of multiple, simultaneous electrosprays. The ESI source opened up new territories for the flowing afterglow technique, involving massive, multiply-charged ions and biomolecules, such as multiply-charged equine cytochrome c ("a little chunk of hamburger flying through a flowing afterglow instrument").

Thermochemical properties: There's nothing like an equilibrium constant

Mountains of useful thermochemical data, including gas-phase acidities, basicities, redox properties and solvation energies, have been derived from gas-phase equilibrium experiments.[12–17] However, not all thermochemical data are amenable to measurement through such experiments. This is especially so for reactive intermediates, such as carbenes, biradicals, and highly unsaturated metal ions—species of particular interest for Bob. Therefore, he employed various alternatives to equilibrium measurements for deriving thermochemical data. These methods ultimately rely on the fact that gas-phase ions are so easily "processed", that is, they are easily moved from one physical location to another, and ion mass-selection allows the complete isolation and identification of particular unimolecular and bimolecular reactions. A few of these thermochemical methods used by Bob and his students are discussed below.

Much of Bob's work over the years dealt with organic negative ions,[18] which naturally led him to consider the gas-phase acidity scale. The gas-phase acidities of neutral molecules (enthalpy change associated with proton loss) normally lie between 300 and 400 kcal mol^{-1}, with the weak acids such as methane and ammonia occupying the top part of the scale, and the strong acids such as HBr and nitric acid occupying the lower part of the scale.[13] Bob and his students determined the acidities of many compounds by employing the so-called bracketing method,[19] wherein one locates the position of the unknown acid on the scale simply by examining its reactions with a series of reference anions having known base strengths. An especially significant study focused on the changes that coordination with common Lewis acid catalysts, such as BH_3 and BF_3, causes in the thermodynamic properties and reactivity of organic molecules.[20] Pronounced effects were found. For example, coordination with BF_3 transforms simple carbonyl compounds into gas-phase *superacids* and *superelectrophiles* with enhancements in acidity of up to 50 kcal mol^{-1} and hydride affinity of up to 66 kcal mol^{-1}. In the condensed phases, changes in acidity of up to 24 pK_a units were estimated by combining the measured gas-phase acidities with the solvation energies computed for these species.

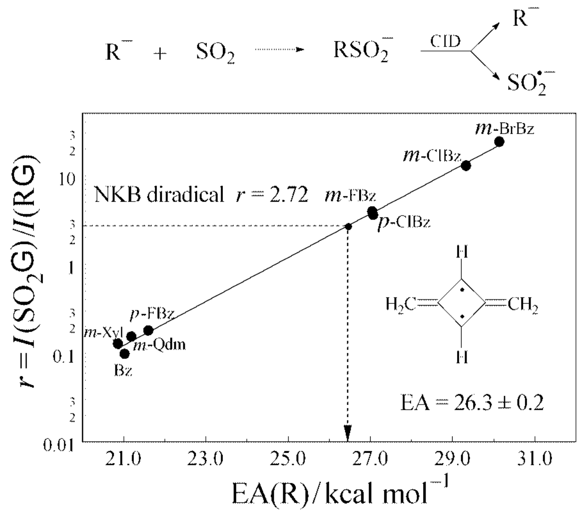


Fig. 3 Determination of the electron affinity of non-Kekulé benzene by CID of the adduct of its carbanion and SO_2.

Another alternative thermochemical approach that Bob often utilized is the kinetic method, which was developed in the mid 1970's by Graham Cooks.[21] In Bob's words, this method involves setting up "a little molecular tug-of-war" between the basic constituents of a proton-bridged cluster ion, the so-called "proton-bound dimer". Dissociation of the proton-bound dimer can be induced, for example, by collisional activation, and the measured yields of the two possible fragment ions can be an exquisitely-sensitive function of the relative proton affinities of the two bases. With careful calibration, the kinetic method can give absolute acidities and basicities with excellent accuracy and precision.[22] It is also quite flexible with respect to the binding element in the cluster ion, which could also be an electron, or a molecular cation or anion. Bob employed this method, for example, for determining electron affinities for radicals,[23] carbenes[24] and biradicals.[25] He found that sulfur dioxide forms abundant adducts with carbanions (R^-) in the flowing afterglow. These adducts undergo CID in the triple quadrupole to produce the carbanion and $SO_2^{-\bullet}$ in yield ratios that display excellent semi-logarithmic correlations with the electron affinities of the corresponding radicals ($R^\bullet$). The electron affinity of the important triplet biradical non-Kekulé benzene (Fig. 3) was determined this way by first generating a calibration plot with a series of benzylic radicals that have accurately known electron affinities, and then determining the yield ratio for the SO_2 adduct of the biradical negative ion.[26]

A major thrust[6] in Bob's lab over the last ten years or so was the determination of thermochemical data from CID threshold measurements.[27] In these experiments, one monitors the yield of a particular CID fragment ion as a function of the center-of-mass collision energy for the reactant ion and neutral target gas, usually argon or xenon. The threshold energy is extracted from the resulting ion appearance plot by fitting the data to a carefully conceived physical model[27,28] that accounts for all available sources of energy in the CID process, as well as possible kinetic shifts in the onset due to slow dissociation. For kinetically well-behaved dissociations with no reverse activation energy, the CID threshold constitutes a direct measurement of

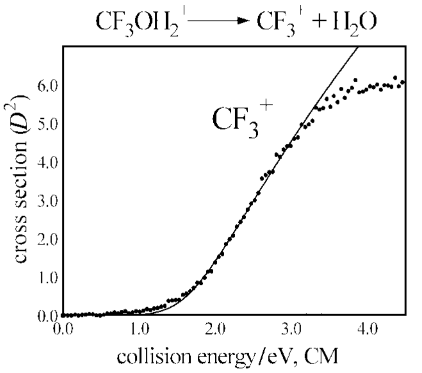


Fig. 4 Determination of the $CF_3–OH_2^+$ bond dissociation energy by CID threshold measurements.

the bond energy and, hence, this method becomes a powerful thermochemical tool. Bob and his students employed this method to carry out the measurement of many important thermochemical values, including solvation energies,[29,30] metal–ligand bond strengths,[31] acid–base properties of extremely weak acids,[32] and heats of formation for reactive ions and neutral species, including several biradicals.[33–35] For example, this approach was used to determine the heat of formation of CF_3OH (Fig. 4), a key intermediate in the atmospheric degradation of hydrofluorocarbons.[36]

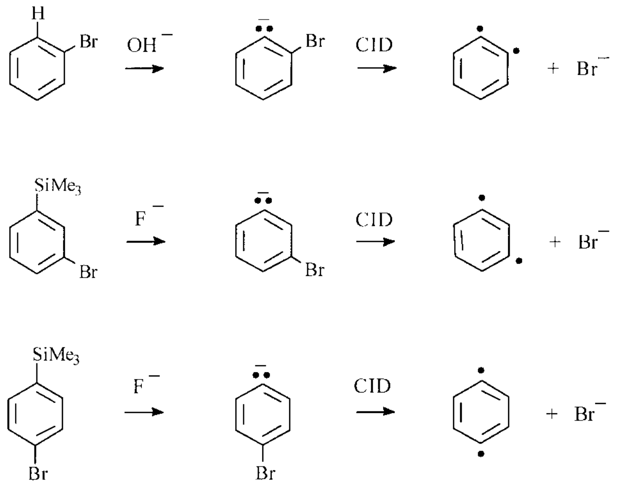
The CID threshold approach proved to be particularly useful for determining the sequential metal–carbonyl bond strengths of transition metal carbonyl ions (Scheme 2; values in kcal mol^{-1}).[31,37] "In these experiments," Bob said, "we whittle the metal ion down, ligand-by-ligand, all the way to the bare atomic metal anion." There are many valuable lessons about electronic structure in these thermochemical data. In a nutshell, when dissociation of a M–CO bond correlates with a product state that is non-optimal for bonding to the remaining ligands, the electronic re-organization energy that must be paid is subtracted from the intrinsic M–CO bond strength. That is, weak metal–ligand bonds are associated with electronic reconfiguration of the products.[38]

$$Fe(CO)_4^- \xrightarrow{42} Fe(CO)_3^- \xrightarrow{42} Fe(CO)_2^- \xrightarrow{36} Fe(CO)^- \xrightarrow{34} Fe^-$$

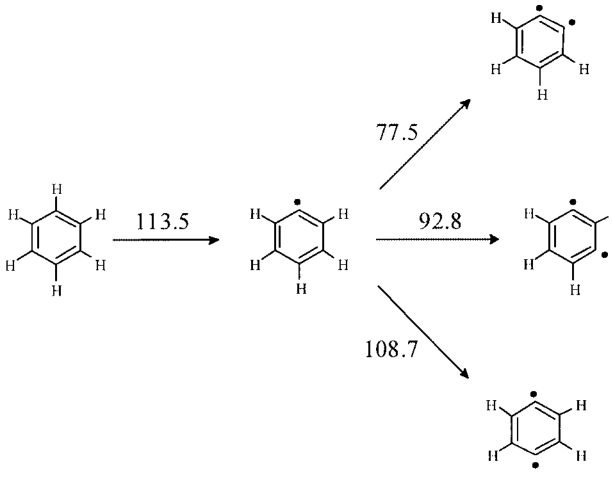
Scheme 2

This approach was also employed to study various interesting organic molecules that have been invoked as transient intermediates in organic reactions, or are found in plasmas, flames, and "swimming around in dense interstellar clouds". Carbynes[33] and carbenes[34,39] were of interest as important organometallic ligands and, as Bob stated, "they are sometimes found clinging to catalytic surfaces." Organic biradicals also attracted his attention,[35,40] partially because some of them play a key role in the antitumor activity of enediyne antibiotics. Bob considered the energetics of these species in terms of sequential CH bond dissociation energies of hydrocarbons. He felt that just as with the metal carbonyls, the sequential CH bond energies of organic compounds yield valuable information on the interplay between electronic structure and thermochemistry. The challenge was to come up with a method to measure these quantities. Bob used CID threshold measurements for this purpose. His work on benzynes, a topic of intense research in his lab for about ten years, is an excellent example of the power of this approach.

For the three isomeric benzynes, the trick was to measure the dissociation energy by CID threshold analysis of ions that produce the benzyne biradicals as neutral products. Various isomeric halophenyl carbanions were synthesized in the flowing afterglow by proton transfer or desilylation reactions.[40] From the measured CID thresholds for loss of bromide (Scheme 3), plus some other measurements, the values were established for the absolute heats of formation of *o*-, *m*- and *p*-benzyne.[40] These quantities were used, along with other data, to derive values for the second CH bond energies in benzene (Scheme 4). The values obtained are much smaller than the first CH bond energy,[41] which indicates significant stabilizing interactions between the radical sites in these three biradicals. This was found to be true even for *p*-benzyne where the radical carbons are more than 2.5 Å away from each other. These results clearly demonstrated that the benzynes are singlet biradicals, wherein the two electrons at the radical sites are spin-paired, so that some bond energy is regained when a second CH bond is broken in benzene. Bob's student Harvey Lardin is now expanding this work to encompass naphthalene CH bonds.



Scheme 3



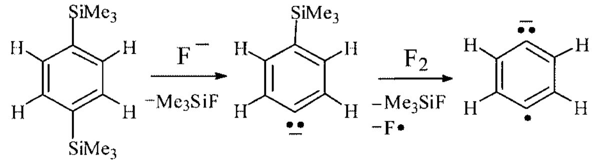
Scheme 4

Synthesis: "If necessity is the mother of invention, then serendipity is its rich uncle."

Much of Bob's efforts over the years focused on figuring out ways to synthesize gaseous ions of practical or theoretical significance. He strived to make and characterize species that had been proposed as transient intermediates in important organic,[35,42–44] inorganic[45,46] and organometallic[47–49] reactions, whose spectroscopic characterization was of fundamental interest,[26,50,51] or whose mere existence was controversial.[52–56] Bob viewed the gas phase as the synthetic chemists' wonderland, because the absence of a reactive medium allows one to create "all kinds of exotic creatures in which the traditional notions of stability are tossed out of the window". While many of the ion synthetic methods that he and his students invented arose from a recognized need and deliberate action, many others were born of complete serendipity: they were looking for one thing, and found another. Bob viewed these occasions as the delightful surprises that make science fun. In this connection, he told his students that his four favorite words in the English language were: "Guess what I made . . .".

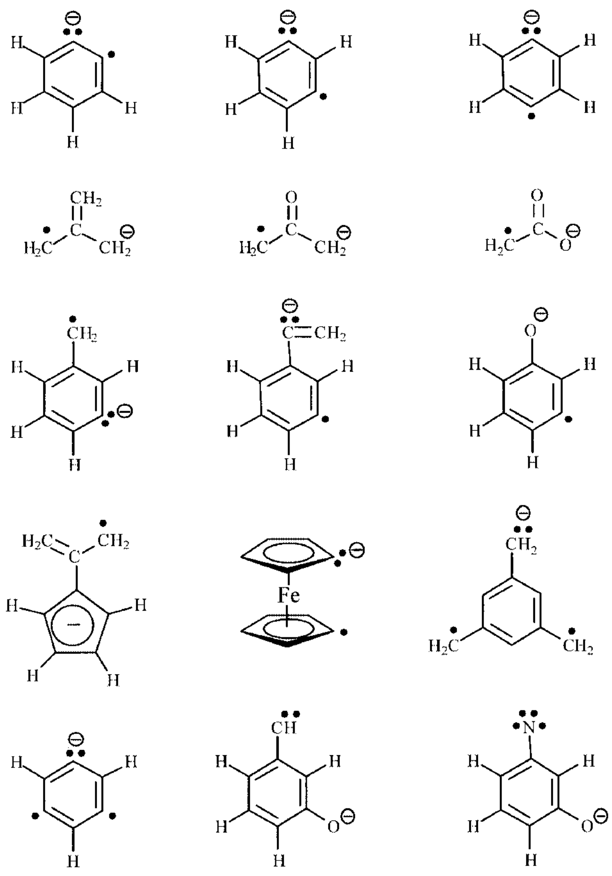
The synthesis strategies developed in Bob's lab include collision-induced decarboxylation for generating highly basic carbanions that cannot be made by any other means.[57,58] This approach was used, for example, to form the neopentyl anion, the only saturated aliphatic alkyl anion other than methyl that has ever been observed. An example of a serendipitous synthesis is the generation of the fascinating class of pentacoordinate silicon hydride ions. In the course of examining the gas-phase ion chemistry of hydride, "a strongly-basic power-packed little ion" that can be made in a flowing afterglow by electron impact on NH_3, Bob and his students discovered that it forms abundant adducts with alkylsilanes.[59,60] Further, they were able to make the archetype of the series, SiH_5^-, by bimolecular hydride transfer to silane.[61] This achievement was especially exciting to theoreticians because of the long history that SiH_5^- had as a model for theoretical studies of hypercoordination and octet-rule violations. As with so many theoreticians' models, it only had an existence in their imaginations and in their computers, until Bob's discovery.

Research on the benzyne biradicals also required the development of clever synthetic strategies when Bob decided that he wanted to obtain information on the magnitude of interaction between the radical sites in benzynes, *i.e.*, the singlet–triplet splitting or the energy difference between the singlet and triplet spin states. The best way to measure these quantities was negative ion photoelectron spectroscopy, an experiment that required intense beams of the negative ion of the biradical of interest. Hence, the measurement of the singlet–triplet gaps of the benzynes began with the synthetic challenge of generation of the isomeric *o*-, *m*- and *p*-benzyne negative ions. The method developed for this purpose is based on the fluoride-induced desilylation procedure developed by Chuck DePuy *et al.* for regiospecific synthesis of gaseous carbanions.[62] The method made use of neutral precursors with two trimethylsilyl groups to define the locations of the negatively-charged and odd-spin sites in the radical anion, and a stepwise reaction sequence in which the first silyl group is removed with fluoride ion, and then the second is removed by a novel reaction with molecular fluorine (Scheme 5).[63] The synthesis worked beautifully, yielding nanoamp currents of the benzyne anions in the flowing afterglow instrument. The photoelectron spectra of these negative ions were measured in a collaborative study with Carl Lineberger, and used to derive the singlet–triplet splittings of the three benzynes, their electron affinities, and vibrational frequencies.[64] Bob's work on the benzynes is generally viewed as a landmark in the field of reactive intermediates.



Scheme 5

Besides benzyne anions, the F_2 procedure was used to generate a broad range of interesting negative ions (Scheme 6),[65] including distonic radical anions of important biradicals, such as trimethylenemethane.[51] The singlet–triplet gap of this molecule was determined by using the same approach as for the benzynes.[66] Removal of three trimethylsilyl groups was employed to form negative ions of triradicals.[67] Molecular fluorine reactions were also found to provide a way to make a new class of distonic carbene ions[44] and distonic nitrene ions[65] whose reactivity is still being examined by Bob's student Brian Hill.

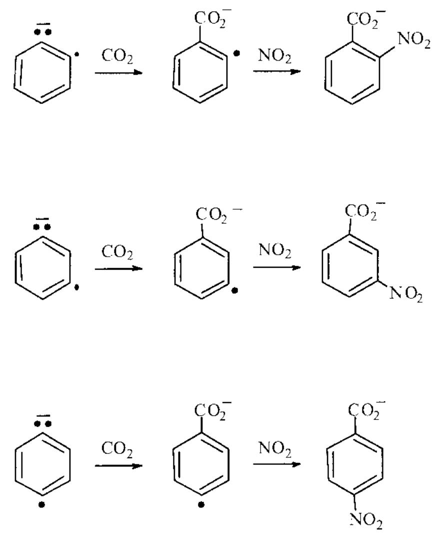


Scheme 6

Structure: "Fancy balance"

With all its tremendous power as a modern structural tool in chemistry, a mass spectrometer is ultimately just a fancy electronic balance. In his talk, Bob described mass spectrometrists as "those who merely weigh things for a living", and continued: "Ah, but the trick is knowing just how to weigh things, and what to do to them before you weigh them." His work demonstrates that if one knows these tricks, one can use the balance to distinguish isomers, tackle stereochemical problems, and even assign likely electronic states to reactive molecules. Bob complemented these studies by very high level molecular orbital calculations.[35,42,50,68] Most of his recent computational studies were carried out in collaboration with Chris Cramer.[69]

Aside from being a valuable thermochemical tool, the kinetic method proved to be an excellent structural tool in Bob's and his students' hands. The kinetic method has been used to measure extremely small differences in proton affinity between molecules—less than a few hundred calories in some cases.[21] To the extent that energy differences can be related to differences in structure, this exquisite sensitivity of the kinetic method can be employed to distinguish subtle differences in molecular structure. For example, chemical reactivity was utterly useless for the structural analysis of the three isomeric benzyne anions because the *meta*- and *para*-isomers behaved identically. Even if this had not been the case, direct reactivity studies on these ions could probably only tell that three ions with different structures had been generated but not specifically what the structures were. To solve this problem, Bob made use of a classical derivatization approach, such as an organic chemist might have used a hundred years ago to identify an unknown compound. He found that, like most carbanions, each of the benzyne anions underwent rapid addition of carbon dioxide to make a dehydrobenzoate ion, which, in a subsequent step, readily coupled with added nitrogen dioxide (Scheme 7). Hence, this procedure converted the three exotic, isomeric anions to a set of mundane, ordinary, everyday nitrobenzoate ions. The kinetic

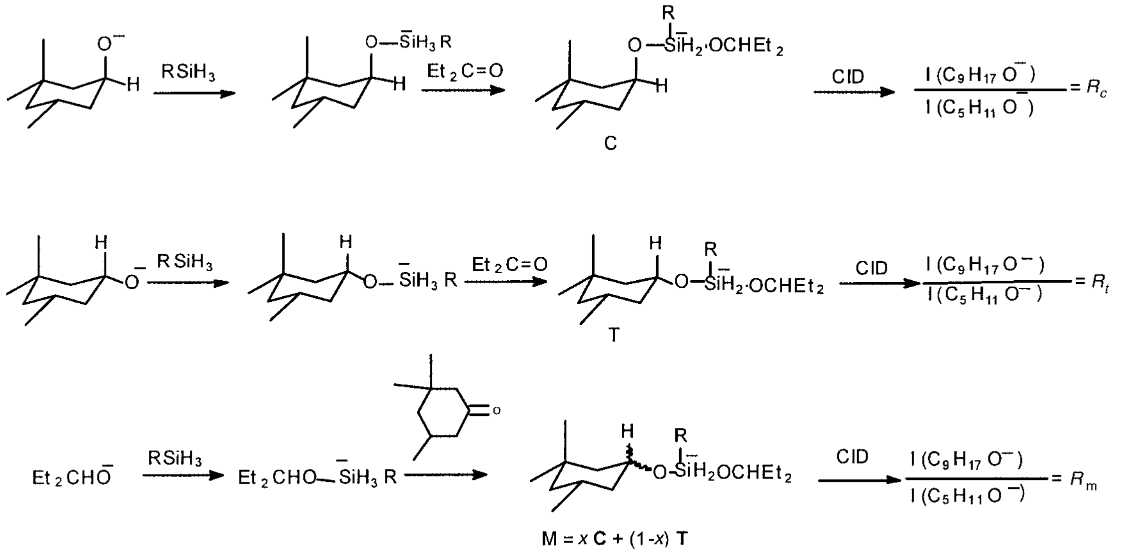


Scheme 7

method was then used to demonstrate that these derivatives were identical to authentic *o*-, *m*- and *p*-nitrobenzoate ions obtained from store-bought neutral acids. This was accomplished by forming a proton-bound dimer of each derivative or authentic ion with difluoroacetic acid, and carefully measuring the characteristic CID yield ratios. The results showed perfect quantitative matches between the CID yield ratios for the derivatives and the authentic ions, and hence proved that correct structures had been assigned for the benzyne anions.[51]

Bob's research on the stereochemical outcomes of gas-phase ion–molecule reactions, and in particular, the important problem of diastereoselectivity in ketone reduction reactions, required the development of tools for stereoisomer distinction. For example, he wanted to know which diastereomeric product is produced from hydride reduction of cyclohexanone derivatives in the gas phase, the *trans* product from axial attack, or the *cis* product from equatorial attack.[59,70] Mountains of data exist for these sorts of reactions in solution. They are mechanistically complex reactions involving polar solvents, oligomeric reagents and many different kinds of reducing agents. Nevertheless, almost all of the predictive theories that have been developed for these reactions are essentially gas-phase conceptual models that focus entirely on the structural and electronic properties of the isolated ketone substrates. Bob decided that it was time for somebody to go ahead and actually measure the diastereoselectivity for the gas-phase reduction reactions in which the reactants really are isolated. This problem required him not only to invent a gas-phase hydride reducing agent, but also to figure out a way to quantitatively analyze mixtures of diastereomeric reduction products, because in general, tandem mass spectrometry does not distinguish diastereomeric alkoxides in a quantitative fashion.

The approach Bob developed[59] relied on two key observations. First, his research on the pentacoordinate silicon hydride ions revealed that they are excellent gas-phase hydride reducing agents.[71,72] For example, monoalkoxy silicon hydride ions, which are easily formed by adding alkoxides to silane, react with aldehydes and ketones by reduction to form a new pentacoordinate silicon ion—a dialkoxysiliconate. That is, reduction occurs by the net addition of a Si–H bond across the carbonyl group of the ketone. Second, these dialkoxysiliconate ions undergo CID by competitive cleavage of the two alkoxide ions, with measurable yield ratios that are exquisitely sensitive functions of the structures and relative basicities of the two fragment ions.[59] This result provided the key to the stereochemical analysis, which then ended up being essentially a Cooks' kinetic method experiment—in this case with a silicon-bound dimer instead of a proton-bound dimer. The protocol was used, for example, to examine the stereochemical outcome of reduction of 3,3,5-trimethylcyclohexanone in the gas phase.[59,70] In this case, 3-pentoxide anion was added to silane to form the monoalkoxysiliconate reducing agent. This ion was then allowed to react with 3,3,5-trimethylcyclohexanone, to form an unknown mixture of the *cis*- and *trans*-reduction products. CID of the diastereomer mixture produced the two alkoxide ions in a specific yield ratio, here referred to as R_m (Scheme 8). Measurement of the separate CID ratios for the authentic *cis*- and *trans*-diastereomers (R_c and R_t) allowed the deduction of the yields of the two diastereomeric product ions in the mixture. This was carried out by reversing the order of the synthesis of the dialkoxysiliconate ions. The authentic *cis*-alkoxide was generated from the commercially available alcohol and added to silane. This ion was used to reduce pentan-3-one to give the authentic *cis*-dialkoxysiliconate (Scheme 8). CID of



$$\% \textit{cis} \text{ product} = x = \frac{(R_m - R_t)(1 + R_c)}{(R_c - R_t)(1 + R_m)} - 100$$

Scheme 8

this ion gave a specific product ion ratio, R_c. The analogous control experiment with the authentic *trans*-alkoxide gave the CID ratio R_t. With the three ratios, R_m, R_c and R_t, and a little algebra, the stereochemical outcome of reduction of 3,3,5-trimethylcyclohexanone was determined to be 91% *cis*-isomer resulting from equatorial attack.

Several ketones were examined this way.[70] The gas-phase stereoselectivities were found to be the same as what is normally observed in solution for these substrates (with one exception, 2-*tert*-butyl-1,3-dioxan-5-one: 33% axial reduction in the gas phase and 93% in solution; this difference was rationalized by electrostatic repulsion between the nucleophilic hydride reagent and the ring heteroatoms in the substrate). Bob was disappointed at this since he had hoped to "upset some old dogma with his shiny new gas-phase results". However, his work led to the important conclusion that reduction diastereoselectivities in solution are likely to be the result of the intrinsic properties of the isolated reactants.

The above study is the last project that Bob brought into completion. Six months after his death, his student Alex Artau completed the manuscript and sent it to the *Journal of the American Chemical Society*. The work was accepted for publication six short weeks later. I believe that the referee's comments nicely reflect the general opinion about Bob's science: "This is an exceptionally good paper, reporting in detail an ingenious method for determining the stereochemistry of hydride reductions in the gas phase"; "This kind of a study has implications for gas phase, solution phase, theoretical, and synthetic organic chemistry". "The authors are to be congratulated on their careful and convincing execution of a very ingeniously designed set of experiments".

Final remarks

Bob's research has left a permanent mark in physical organic chemistry and gas-phase ion chemistry. His work is characterized by brilliant scientific thinking and an uncompromising, intense approach to science—endless curiosity, deep respect for nature, not accepting a problem addressed unless it is thoroughly understood. For many of us, he was the hardest critic and, at the same time, the strongest supporter. Knowing Bob inspired us to raise our standards and to strive for more serious understanding. To me, that is his legacy.

Acknowledgements

I wish to thank Bob's current students, Brian Hill, Alex Artau and Harvey Lardin, as well as Paul Wenthold, Ian Rothwell, Graham Cooks, Wes Borden and Chris Cramer, for reading the manuscript and providing valuable comments.

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