



# **Studies in Gas Phase Ion Chemistry**

**A thesis presented for the degree of**

**Doctor of Science**

**in**

**The Faculty of Science**

**of**

**The University of Adelaide**

**by**

**Richard Alfred John O'Hair**

**B.Sc.(First Class Honours) 1986, Ph.D. (Adelaide) 1991**

**December 2004**

**Dedicated to Antoinette and Carmel**

*"I do not know what I may appear to the world; but to myself I seem to have been only like a boy playing on the sea-shore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me."*

**Sir Isaac Newton (1642-1727)**

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## Copies of Publications:

Publications (A): Gas Phase Ion-Chemistry and Mass Spectrometry of Biomolecules

Publications (B): Inorganic and Organometallic Gas Phase Ion Chemistry

Publications (C): Organic Gas Phase Ion Chemistry

Publications (D): International Patent

Publications (E): Invited Reviews

Publications (F): Invited Book Chapters

Publications (G): Invited Encyclopedia Contributions

Publications (H): Other Invited Scientific Publications

## Summary Supporting Claim for D.Sc.

The research described in this thesis represents a broad study of the gas phase ion chemistry of biomolecules, inorganic, organic and organometallic species. The unifying theme for many of these studies is the use of advanced mass spectrometry techniques coupled with theoretical calculations to gain detailed insights into structure, mechanisms and reactivity.

The first section reports on the gas phase ion-chemistry and mass spectrometry of biomolecules. This broad research area is further categorised into the sub areas of: Thermochemistry; Regioselectivity of alkylation reactions; Ion-molecule reactions as structural probes; Mechanisms of dissociation reactions of protonated and deprotonated peptides and oligonucleotides; Reactivity of radicals derived from peptides and oligonucleotides; Structure and reactivity of metallated peptides; Reactivity of non-covalent complexes; Analytical applications. Specific highlights include: the experimental determination of the gas phase acidities of the  $\alpha$  amino acids; the development of a detailed understanding of the fundamental gas phase fragmentation mechanisms of  $\alpha$  amino acids and peptides to the stage that a new proteomics approach has been patented; carrying out some of the first gas phase ion-molecule reactions of non-covalent complexes of biomolecules which demonstrate molecular recognition.

The second section describes inorganic and organometallic gas phase ion chemistry studies and is further categorised into the sub areas of: reactions of organosilicon, organophosphorus and organosulfur species; gas phase coordination chemistry of platinum; insights into catalysis by transition metal oxides and peroxides; synthesis and reactivity of organometallics. Specific highlights include: the discovery of a number of catalytic cycles; showing that collision-induced dissociation can be used to "synthesise" gas phase organometallic species for subsequent reactivity studies. Examples of catalysis include: oxidation of alcohols by the dimolybdate anion,  $[\text{Mo}_2\text{O}_6(\text{OH})]^-$ ; dehydration of acetic acid by group VI metal oxide anions,  $[\text{MO}_3(\text{OH})]^-$  and  $[\text{M}_2\text{O}_6(\text{OH})]^-$  ( $\text{M} = \text{Mo}$  and  $\text{W}$ ); decarboxylation of acetic acid by the organomagnesate  $\text{CH}_3\text{MgCl}_2^-$ . The organometallic studies have revealed that: while the organocuprate  $(\text{CH}_3)_2\text{Cu}^-$  reacts with methyl iodide via a C-C bond coupling reaction (occurring via a "T shaped" transition state), its silver congener is unreactive; the organomagnesates,  $\text{CH}_3\text{MgL}_2^-$  ( $\text{L} = \text{Cl}$  and  $\text{O}_2\text{CCH}_3$ ) show some of the reactivity of Grignard reagents, but fail to undergo the Grignard reaction. The subvalent silver hydride cluster,  $\text{Ag}_4\text{H}^+$ , has been assembled in a unique fashion from silver amino acid precursor, and has been shown to mediate the C-C bond coupling of allylbromide.

The final section reports on the gas phase ion-chemistry of organic species and is further categorised into: thermochemistry; mechanisms of ion-molecule reactions; formation of unusual species and reactive intermediates. An important finding on the mechanisms of substitution reactions at  $sp^2$  hybridised C atoms shows that while acyl pyridinium ions can undergo substitution, aryl diazonium ions appear to be unreactive in the gas phase.

## Acknowledgments

I have been very fortunate to have two very supportive mentors: Professors John Bowie and Charles DePuy. Both allowed me a large amount of freedom during my PhD and postdoctoral studies, encouraging me to pursue my own ideas, thus laying the foundations of my academic career. Thank you John and Chuck!

Most of the research described in this thesis was carried out during my independent academic career at the Department of Chemistry of Kansas State University and the School of Chemistry of The University of Melbourne. This work would not have been possible without the input from a number of talented graduate and undergraduate students, whose names appear on the publications listed in this thesis. This research has been a shared journey for all of us, and I have continued to learn from every new project. I want to single out the following for their specific contributions: Mike Freitas for enthusiastically adopting physical organic chemistry approaches to understanding the gas phase alkylation reactions of models for biomolecules, even though he was enrolled as an analytical chemistry student. Mike also embraced the opportunity to travel to Melbourne to complete his PhD while also helping to set up the new laboratory there. Michelle Styles and Gavin Reid were my first PhD students at Melbourne and welcomed carrying out research with a new faculty member, even though that meant helping to set up a new laboratory. Gavin was keen to study the fragmentation reactions of protonated peptides. Although this was a logical extension from Mike's gas phase alkylation reaction studies, I was a bit dubious at first given the vast number of studies in the literature. Nonetheless, we were able to uncover a number of new reactions and also revise a number of incorrect mechanisms. The fact that Gavin was able to finish his PhD thesis in two and a half years, speaks volumes about his enthusiasm, energy and professional dedication to his research work. Both Mike and Gavin have moved into academic careers in the USA and, like a proud father, I look forward to their contributions to science. More recently I have had a number of enthusiastic and talented students (Ana Vkrlic, Sheena Wee, Tom Waters, Chris Barlow and Pat James) who have helped steer our research into the areas of inorganic, bioinorganic and organometallic chemistry.

I would like to acknowledge the following academic staff for their advice, support and encouragement: (a) at Kansas State: Don Setser and Ken Klabunde; (b) at Melbourne: Don Cameron, Carl Schiesser and Ken Ghiggino. A number of my studies have involved collaborations with other academics and their research teams. Their names appear on the publications listed in this thesis. I want to single out and warmly thank the following: Scott

Gronert (San Francisco State University); David McFadyen and Tony Wedd (University of Melbourne); Todd Williams (University of Kansas) and Peter Armentrout (University of Utah). Perhaps the biggest thanks goes to Scott McLuckey who introduced me to the wonderful world of quadrupole ion traps during my sabbatical leave at Oak Ridge National laboratories.

Any researcher who uses advanced spectroscopic instruments as a mainstay of their research, knows that things would soon grind to a halt without the help and important input from the support staff in the workshops (electronic, mechanical and computing). I thank all support staff at both Kansas State University and The University of Melbourne, for helping to trouble-shoot problems and repair our instruments.

Finally, my journey as an academic would not have been possible without the continuous support and encouragement from my wife Antoinette. You have been my muse for nearly 20 years and have helped a drifting and disinterested chemical engineering student to become re-invigorated and re-discover the joys of chemistry.



## Detailed Curriculum vitae

### Personal Information

Date of Birth: December 28, 1964  
Nationality: USA and Australian  
Marital Status: Married, one daughter (born May 24, 1998)  
Languages: English and German

### Education

B.S. (Top 1st class Honours), University of Adelaide, 1986.  
Ph.D., University of Adelaide, 1991.

### Research Experience

1/2003-present Associate Professor and Reader, School of Chemistry, The University of Melbourne, Victoria, Australia  
8/1996-12/2002 Senior Lecturer, School of Chemistry, The University of Melbourne, Victoria, Australia  
5/1996-8/1996 U.S. Department of Energy (DOE) Faculty Research Fellow at Oak Ridge National Laboratory (Oak Ridge, Tennessee)  
8/1993-5/1996 Assistant Professor, Department of Chemistry, Kansas State University, Kansas, USA  
7/1991-7/1993 Postdoctoral Research Fellow, Department of Chemistry & Biochemistry, University of Colorado at Boulder, USA  
1-7/1991 Postdoctoral Research Fellow, Department of Organic Chemistry The University of Adelaide, South Australia, Australia  
1/1990-1/1991 Postdoctoral Research Associate, Chemistry Department, University of Wollongong, New South Wales, Australia

### Awards, Scholarships and Honours

2004 Elected Fellow of the Royal Australian Chemical Institute (FRACI)  
2002 Gilmour Research Award  
2001 David Syme Research Prize  
2001 The Royal Society of Chemistry Travel Award  
1998 The Selby Research Award  
1996 U.S. Department of Energy (DOE) Faculty Research Fellowship at Oak Ridge National Laboratory (Oak Ridge, Tennessee)  
1991 Australian Research Council Postdoctoral Research Fellowship  
1988 The Heddle Research Award  
The University of Adelaide Travel Scholarship to the University of Colorado at Boulder, USA  
1987 Commonwealth Postgraduate Scholarship  
1986 The Rennie Scholarship for Distinction in Chemical Research  
Commended for Achieving the Top First Class Honours in Organic Chemistry

## Research Funding

- Since August of 1996, I have attracted over A\$1,000,000 worth of internal and external funding.
- Australian Research Council funding includes three single investigator three year Large/ Discovery grants, a joint Discovery grant and a Lief grant.

## Research Publications

- Over 110 scientific publications in peer reviewed journals, of which more than 70 are the result of my own independent research program.
- The only Australian scientist to have published in the first volume of the Encyclopaedia of Mass Spectrometry (published in 2003)
- 10 reviews/book chapters, including invited reviews on the mass spectrometry of organophosphorus compounds, published in the book: "The Chemistry of Organophosphorus Compounds - Volume 4" and ion chemistry and fragmentation in the book "Mass Spectrometry in Drug Discovery".

## Research Presentations

- Over 70 scientific research presentations from our group, including conference presentations as well as invited lectures (recently including 3 invited keynote lectures and 3 plenary lectures at international conferences).

## Research Training of Graduate and Undergraduate Students

During my independent research program, I have supervised the research of 2 graduate (1 MS and 1 PhD) and 2 undergraduate students at Kansas State University (8/1993-5/1996) and 7 PhD students and over 20 honours and undergraduate students at the University of Melbourne.

The following postgraduate students have been awarded their thesis:

### Kansas State University:

- Jacob D. Smith (M.S., graduated in 1996) MS Thesis Title: "Gas-Phase Ion Studies of Sulfur and Phosphorus Containing Molecules"
- Michael A. Freitas (Ph.D., graduated in 1997) PhD Thesis Title: "A Study of the Gas-Phase Reactivity of Model Biomolecules with Cationic Electrophiles"

### University of Melbourne

- Michelle A. Styles (Ph.D. candidate 1997-2001) PhD Thesis Title: "Gas-Phase Studies of Biomolecules Complexed to Ligated Platinum (II) Derivatives"
- Gavin Reid (Ph.D. candidate 1998-2000; joint student with Simpson) PhD Thesis Title: "Studies on the Fragmentation Reactions of Protonated Amino Acids and Peptides by Tandem Mass Spectrometry and Gas-Phase Ion-Molecule Reactions"
- Ana Vrik (Ph.D. candidate 1999-2004) PhD Thesis Title: "Gas-Phase Reactivity Studies of Non-Covalent Complexes, Diazonium Ions and Grignard Reagents"
- Tom Waters (Ph.D. candidate 2000-2004; joint student with Wedd) PhD Thesis Title: "Gas-Phase Studies of Metal-Oxo Ions"
- Sheena Wee (Ph.D. candidate 2001-2004; joint student with McFadyen) PhD Thesis Title: "Gas-Phase Studies of Metal Complexes of Biomolecules"
- Hadi Lioe (Ph.D. candidate 2003- ; joint student with Reid)
- Christopher Barlow (Ph.D. candidate 2004- ; joint student with McFadyen)

## Membership of Professional Associations

- Royal Australian Chemical Institute (Elected Fellow in 2004)
- American Chemical Society
- Australian and New Zealand Society for Mass Spectrometry
- Melbourne University Chemical Society
- American Society for Mass Spectrometry

## Service to Chemistry Community

I am actively involved on a range of committees, serve on four editorial advisory boards of international scientific journals and participate in many other activities including:

- |              |                                                                                                                                                                                                                               |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2004         | Editorial Advisory Board Member "Journal of the American Society for Mass Spectrometry"                                                                                                                                       |
| 2004         | Editorial Advisory Board Member "Rapid Communications in Mass Spectrometry"                                                                                                                                                   |
| 2004         | VCE Chemistry Review Committee (Charged with the responsibility of developing a new Victorian curricula of year 11 and 12 High School Chemistry)                                                                              |
| 2003         | VCE Science Expert Advisory Studies Committee (Charged with the responsibility of making recommendations on the review of the Victorian curricula of year 11 and 12 High School Chemistry, Biology and Environmental Science) |
| 2003         | Guest Editor for the Professor John H Bowie Honour issue of the Australian Journal of Chemistry                                                                                                                               |
| 2003         | Guest Editor for a special issue of the European Journal of Mass Spectrometry                                                                                                                                                 |
| 2000–present | Editorial Advisory Board Member "International Journal of Mass Spectrometry"                                                                                                                                                  |
| 1995–present | Editorial Advisory Board Member "European Journal of Mass Spectrometry"                                                                                                                                                       |
| 2002–present | Vice President of the Australian and New Zealand Society for Mass Spectrometry.                                                                                                                                               |
| 2001–2003    | Convenor of the 19 <sup>th</sup> Meeting of the Australian and New Zealand Society for Mass Spectrometry (held in Lorne, Feb. 2-6, 2003).                                                                                     |
| 1997–2001    | Secretary of the Australian and New Zealand Society for Mass Spectrometry.                                                                                                                                                    |
| 1997         | Secretary of the Melbourne University Chemical Society                                                                                                                                                                        |
| 1997-present | Mass spectrometry consulting for various industrial chemical companies in Australia (including ICI Australia (now Orica))                                                                                                     |

Reviewer for numerous Journals, PhD theses and international funding agencies. Journals include:

- *Journal of the American Chemical Society*
- *Journal of Physical Chemistry (A and B)*
- *Journal of Organic Chemistry*
- *Inorganic Chemistry*
- *Dalton Transactions*
- *Organic and Biological Chemistry*
- *Angewandte Chemie International Edition*

- *International Journal of Mass Spectrometry*
- *Journal of the American Society for Mass Spectrometry*
- *Rapid Communications in Mass Spectrometry*
- *Journal of Mass Spectrometry*
- *European Journal of Mass Spectrometry*

Funding agencies include:

- *Australian Research Council*
- *National Science Foundation (USA)*
- *Petroleum Research Fund (USA)*
- *Research Corporation (USA)*
- *Wellcome Trust (UK)*

#### **Military Service**

- Service in the Australian Army Reserve, Adelaide University Regiment

#### **Publications:**

***PhD Thesis, Department of Organic Chemistry, University of Adelaide, (submitted December, 1989, awarded 1991): "Reactions of Selected Organic, Organosilicon and Organophosphorus Anions in the Gas Phase."***

#### **Publications in Refereed Journals and Books**

- [1] O'Hair, R. A.; Bowie, J. H.; Currie, G. J., "Collision-induced Dissociations of Negative Ions Formed by Reaction of HO<sup>-</sup> with Alkyl and Aryl Silanes. The Formation of Multiple Bonds to Silicon", *Aust. J. Chem.*, **1988**, *41*, 57-67.
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- \* "Gas Phase Ion Chemistry of Biomolecules. Part 6"
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- Electrospray Ionization Mass Spectrometry.", *Eur. Mass Spectrom.*, **1997**, 3, 390–395.
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**Other Publications:**

- [O1] **Book Review:** O'Hair, R. A. J.; Derrick, P.J, *Eur. J. Mass Spectrom.*, **2002**, *8*, 333-335, review of "Interpreting Protein Mass Spectra" by A Peter Snyder, Published by Oxford University Press Inc, New York, USA, Copyright 2000 ISBN 0-841-23571-6.
- [O2] **News and Views Announcement:** Green, A.; O'Hair, R. A. J.; "Professor John Bowie Festschrift." *Chemistry in Australia*, **2003**, *70*(4, May Issue), 36.
- [O3] **Editorial and Biographical Sketch:** O'Hair, R. A. J.; "John Hamilton Bowie: An Appreciation" *Aust. J. Chem.*, **2003**, *56*, 343-348.
- [O4] **Editorial and Historical Sketch:** O'Hair, R. A. J.; "The Australian and New Zealand Society for Mass Spectrometry Conference – A Tradition of Over Thirty Years." *Eur. J. Mass Spectrom.*, **2003**, *9*, 525-529.

**Patent:**

- [P1] **International Patent PCT Int. Appl. WO 2004046731. Title of Invention:** Method for analysing amino acids, peptides and proteins; **Inventors:** Reid, G. E.; Simpson, R. J.; O'Hair, R. A. J. Awarded 2004 and listed in Chemical Abstracts as CAN 140: 420 396.

**Numismatic Publications:**

- [N1] O'Hair, R. A. J., "A New Die Error in the Silver Second Coinage of Henry VIII.", *Numismatic Circular.*, **1997**, *105*, 283.
- [N2] O'Hair, R. A. J.; Tordesillas, A. "Contemporary evidence for siege coins: Hermannus Hugo's journal on the siege of Breda of 1624-1625.", *Journal of the Numismatic Association of Australia*, **2000**, *11*, 50-54.
- [N3] O'Hair, R. A. J.; Tordesillas, A. "Aristocrats of Crime: The hulk token of George Barrington and David Brown Dignam.", *Journal of the Numismatic Association of Australia*, **2002**, *13*, 7-18. NOTES: (i) token made the cover of the journal; (ii) this article resulted in the award of the Ray Jewell Medal for best Numismatic Article published in the *Journal of the Numismatic Association of Australia* over the past two years.

*"In pure science it is a matter of ten or fifteen years before work begins to bear fruit and the scientist must share the patience of the orchardist."*

**William Sutherland (quoted by W.A. Osborne in 'William Sutherland – A Biography', Lothian Book Publishing Co., Melbourne, 1920, page 46).**



## Account of the Research

### Overview:

Many chemical reactions of ionic species occur in solution, but understanding them in detail is complicated by the presence of solvent molecules and counter ions. Mass spectrometry (MS) offers an opportunity to examine ionic reactions in a pristine gas phase environment, where solvent molecules and counter ions are absent. Theoretical chemistry provides a perfect adjunct to MS experiments, as the structures and energies of key species on the potential energy surfaces of reactions can be explored. Over the past decade, we have used a combination of advanced MS techniques, in conjunction with *ab initio* and DFT calculations, to examine the three main areas detailed below: *gas phase ion-chemistry and mass spectrometry of biomolecules; inorganic and organometallic gas phase ion chemistry; and organic gas phase ion chemistry.*

### ***ESI-QIT-MS: a “complete gas phase chemical laboratory:”***

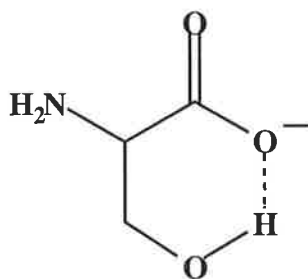
All mass spectrometers consist of: (i) an ionization source; (ii) a mass analyzer; (iii) a detector; (iv) a data recorder/processor. Of all the many combinations of ionization source and mass analyzer, the marriage of two Nobel prize winning technologies (electrospray ionization (ESI) and quadrupole ion traps) has resulted in a powerful and versatile instrument. ESI, developed by John Fenn (2002 Nobel Prize in Chemistry) is a “soft” ionization technique, in which ions are transferred from solution into the gas phase. It is broadly applicable to any organic, inorganic, organometallic and biological molecule which can form a charged species. The QIT, invented by Wolfgang Paul (1989 Nobel Prize in Physics), is a versatile mass analyzer which offers multistage mass spectrometry (MS<sup>n</sup>) capabilities and the capacity to perform collision induced dissociation (CID), ion-molecule reactions and even ion-ion reactions. Since arriving at Melbourne in late 1996, our group is only one of a handful around the world to have successfully modified a commercial quadrupole ion trap mass spectrometer to allow gas phase ion-molecule reactions of ions generated via ESI to be examined. This instrument takes advantage of the “treasure trove” of interesting ions which can be formed via ESI, as well as the multistage mass spectrometry (MS<sup>n</sup>) capabilities of the ion trap, to provide a powerful complete gas phase chemical laboratory in which ions can be manipulated and studied in a sequence of reactions. Much of the work described below was carried out on this instrument.

### **(A) Gas Phase Ion-Chemistry and Mass Spectrometry of Biomolecules:**

This broad area of research has focussed on fundamental and applied studies of biomolecules and related model systems and has led to over 40 publications in the series “The Gas Phase Ion Chemistry of Biomolecules”. The results of these studies have important ramifications for improving the analysis of biologically important molecules via

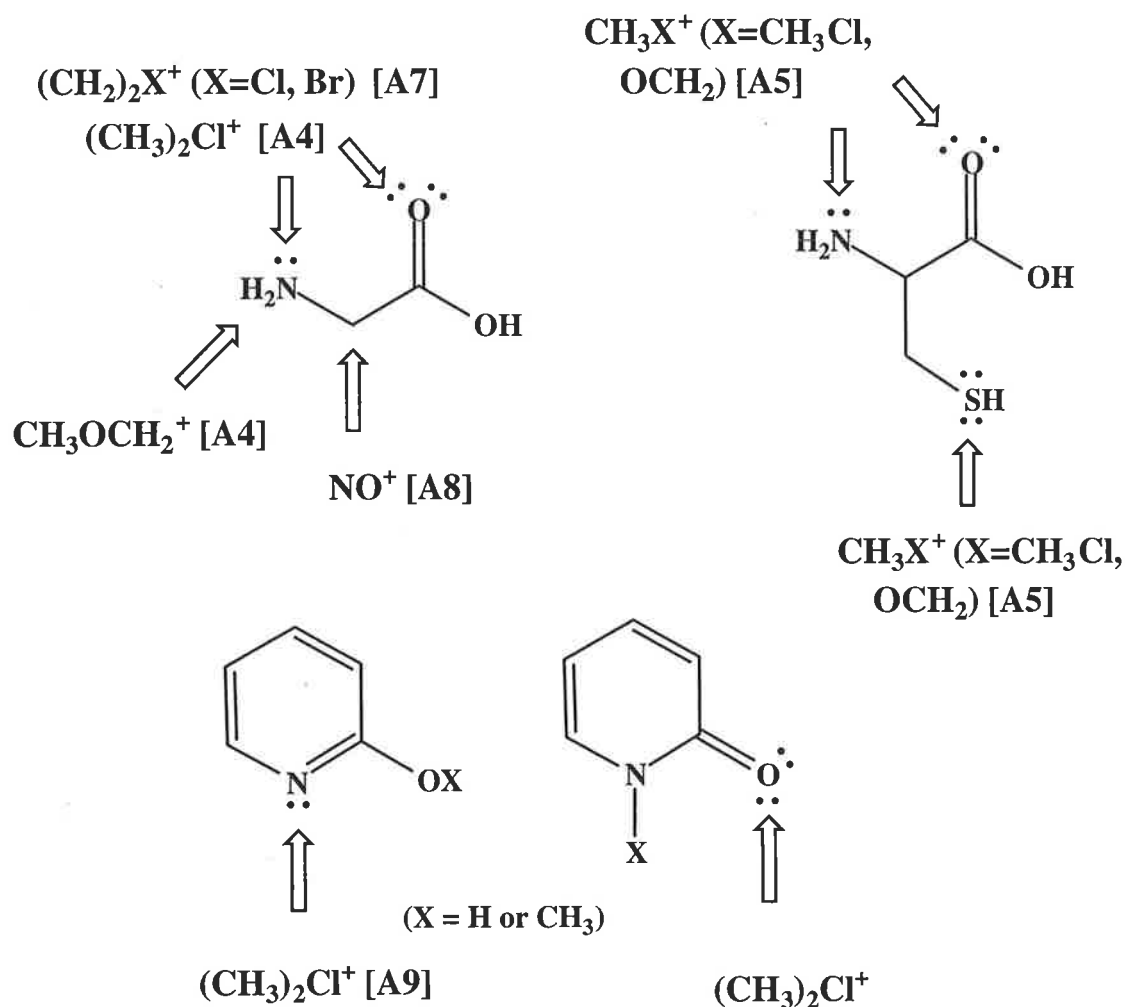
tandem mass spectrometric techniques, as demonstrated by the granting of a patent [D1]. Key results in the following sub areas are now discussed:

**(1) Thermochemistry.** The kinetic method in conjunction with *ab initio* calculations (carried out in collaboration with Professor Gronert) has been applied to examine the gas phase acidities of the  $\alpha$  amino acids [A1] and how isotopic substitution influences the proton affinity of glycine [A2]. Both experiment and theory agree that serine and cysteine are more acidic than glycine. The *ab initio* calculations reveal the structural features that cause the acidity increase. In the case of serine, the product structure **1** is formed, in which the carboxylate anion is stabilized via intramolecular solvation with the side chain hydroxyl group. In contrast, the enhanced acidity of cysteine is due to the polarizability of the thiol group. Although isotopic substitution might be expected to result in only a small change in the gas phase proton affinity or acidity of a species, very few studies had examined this phenomenon experimentally. Using the kinetic method, the effect of deuterium and  $^{15}\text{N}$  labelling on the gas phase proton affinity of glycine was examined. The following proton affinity order was found:  $\text{PA}(\text{H}_2\text{NCD}_2\text{CO}_2\text{H}) > \text{PA}(\text{H}_2^{15}\text{NCH}_2\text{CO}_2\text{H}) > \text{PA}(\text{H}_2\text{NCH}_2\text{CO}_2\text{H})$ . *Ab initio* calculations carried out by Professor Gronert revealed that the cause of this proton affinity order is the change in zero point energies, brought about by isotopic substitution. Both of these experimental studies [A1,A2] raised interesting questions about the conformations of amino acids in the gas phase, and this was probed in a follow up theoretical paper (also in collaboration with Professor Gronert), which examined the neutral conformations of glycine, serine and cysteine [A3]. These fundamental studies have attracted considerable interest, and papers [A1] and [A3] have been well cited in the literature.



**1**

**(2) Regioselectivity of alkylation reactions.** Biomolecules, such as proteins and DNA, can be damaged by reactions with electrophiles or radicals. Using a combination of chemical ionization tandem mass spectrometry, kinetic studies, and *ab initio* calculations, we have examined the gas phase reactions of organic and inorganic electrophiles with simple models of biomolecules and the results of these studies are summarized in Figure 1 [A4-A9].



**Figure 1:** Sites of attack by electrophiles onto small models for biomolecules in CI/MS/MS experiments (references to specific papers in square brackets).

Glycine exhibits diverse reactivity towards electrophiles, with the dimethylchlorinium ion ( $(\text{CH}_3)_2\text{Cl}^+$ ) [A4] and cyclic ethylene halonium ions ( $(\text{CH}_2)_2\text{X}^+$ , where  $\text{X} = \text{Cl}, \text{Br}$ ) [A7] alkylating at both nitrogen and oxygen; methoxymethyl cation ( $\text{CH}_3\text{OCH}_2^+$ ) undergoing regioselective attack at the nitrogen with elimination of methanol to form a  $[\text{M}+\text{CH}]^+$  ion [A4]; nitrosonium ion,  $\text{NO}^+$ , abstracting a hydride ion from the  $\alpha$  carbon to form the iminium ion,  $[\text{H}_2\text{NCHCO}_2\text{H}]^+$  [A8]. The reactivity of cysteine with the dimethylchlorinium ion,  $(\text{CH}_3)_2\text{Cl}^+$ , and the methoxymethyl cation,  $\text{CH}_3\text{OCH}_2^+$ , are even more complex, with different regioselectivity for the formation of the  $[\text{M}+\text{CH}_3]^+$  ions occurring [A5]. For the dimethylchlorinium ion, methylation occurs at all sites, with the degree of methylation at each site following the order:  $\text{N} > \text{S} > \text{O}$ . In contrast, the degree of methylation at each site follows the order:  $\text{S} > \text{N} > \text{O}$  for the methoxymethyl cation. Given the interesting behaviour of the methoxymethyl cation ( $\text{CH}_3\text{OCH}_2^+$ ) as an ambident

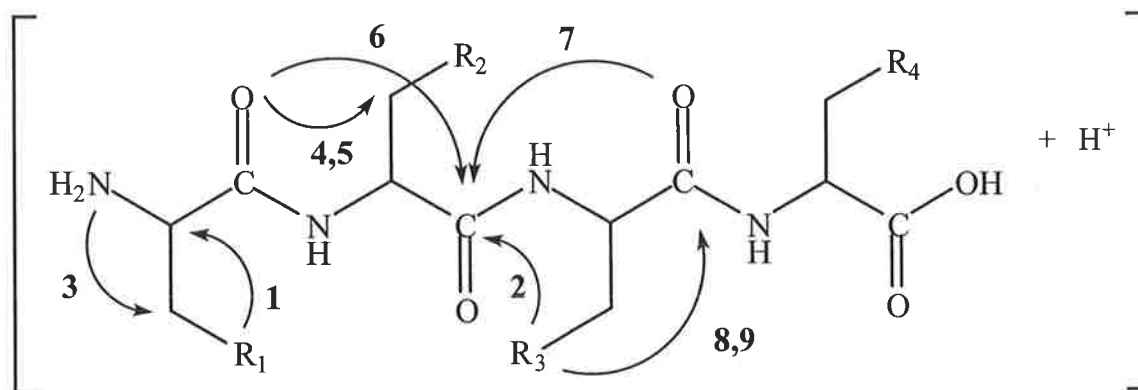
electrophile, its reactions with 21 nucleophiles of different classes (alcohol, ethers, thiols, thioethers, aliphatic ketones, acids, esters and amides, as well as the following aromatics: benzene, pyridine and aniline) were quantified via kinetic studies in a flowing afterglow apparatus [A6]. Three general types of reaction channels were observed: addition followed by elimination of methanol with concomitant  $[M+CH]^+$  ion formation;  $S_N2$  methylation, resulting in  $[M+CH_3]^+$  ion formation; and adduct ( $[M+CH_3OCH_2]^+$ ) formation. Formamide and N,N-dimethylformamide both yield additional products, arising from cleavage of the amide bond by  $CH_3OCH_2^+$ . Finally, the gas-phase methylation of the 2-hydroxypyridine/2-pyridone system by the dimethylchlorinium ion was used as a model for alkylation of the nucleobase sites in DNA [A9]. Alkylation was selective for each tautomer, with 2-hydroxypyridine preferring to methylate on nitrogen, while 2-pyridone underwent methylation on oxygen (Figure 1).

**(3) Ion-molecule reactions as structural probes.** A logical extension of the alkylation reactions discussed above, was their use as probes for the structures of biomolecules. Since  $CH_3OCH_2^+$  was shown to cleave the amide bonds in formamide and N,N-dimethylformamide [A6], we examined its reactions with peptides [A10]. While free peptides underwent reaction at the N terminal amine (consistent with the reactivity of glycine [A4]), the high reactivity of this site could be tempered by N-acetylation, allowing the methoxymethyl cation to cleave peptide bonds in the gas phase. The distinction of isomeric peptides was demonstrated [A10]. A follow up theoretical study found that the substituted methyl cations  $XCH_2^+$  ( $X = OH, F \text{ \& \ } Cl$ ) can add at both the oxygen (thermodynamically favored) and the nitrogen atoms of the amide group of formamide, but that only the N adduct fragments via cleavage of the amide bond [A11]. Alternative peptide bond cleavage reactions were examined [A12, 13]. Rather than undergoing transacylation reactions, protonated peptides were found to react with amines via proton transfer [A12]. In contrast, ion-molecule reactions of neutral peptides with charged acylium ions result in cleavage of the N-terminal amino acid in a reaction reminiscent of the Edman Degradation [A13]. Alternatively, the N-terminus of peptides can be derivatized via a gas phase ion-molecule reaction between protonated peptides and acetone, resulting in Schiff's base formation [A14]. The advent of ESI has opened up the possibility of studying the gas phase ion-molecule reactions of dianions derived from biomolecules with reactive neutral electrophiles. During a sabbatical visit at Oak Ridge National Laboratories, I examined the trimethylsilyl derivatization of nucleic acid anions in the gas phase [A15]. Three types of reactions were observed when nucleic acid anions,  $[M-nH]^n-$ , were allowed to react with trimethylsilylchloride: (i)  $S_N2(Si)$  when  $n > 1$ ; (ii) adduct formation when  $n = 1$  and (iii) addition followed by elimination of HCl when  $n = 1$  and where an acidic phosphate proton is present (eg dA-5'- $PO_3H$ ). CID reactions are consistent with trimethylsilyl attachment on

the phosphodiester linkage(s) in oligonucleotides and on the phosphate moieties of dA-5'-PO<sub>3</sub>H and dA-5'-TP.

**(4) Mechanisms of dissociation reactions of protonated and deprotonated peptides and oligonucleotides:** A number of the ion-molecule reaction studies discussed above in (2) and (3) required using MS/MS studies to interrogate the site of reaction by understanding the gas phase fragmentation behaviour of the charged biomolecule. This triggered studies aimed at the development of a “toolbox” and a conceptual framework to understand the gas phase fragmentation mechanisms of amino acids, peptides and DNA models [A16-A34]. Most of the key ideas and mechanistic pathways have been discussed in an invited mini review [E3]. Perhaps the most significant idea is that many of the gas phase fragmentation reactions of protonated amino acids and peptides involve intramolecular reactions, in which a neighbouring nucleophile attacks a nearby electrophilic site, to facilitate bond cleavage to yield either sequence or non-sequence ions (Scheme 1). While such neighbouring group reactions are well-known in condensed phase solvolyses reactions of organic substrates, their involvement in protonated peptide fragmentation reactions were not fully appreciated. Some of these reactions were discovered by the use of model systems, while others were confirmed in a collaborative study with Professor Simpson's research group (Ludwig Institute for Cancer Research), in which a database of tryptic peptides was “mined” [A26]. Taken as a whole, these studies have important implications for the practical applications of mass spectrometry to proteomics. Apart from the possibility of refining search algorithms for programs that interrogate MS/MS sequencing data, a detailed understanding of peptide fragmentation mechanisms opens the door to controlling gas phase fragmentation reactions of specifically engineered derivatives of peptides. For example, the conversion (via alkylation) of methionine to fixed charge methionine sulfonium ions results in selective loss of the side chain. This and related strategies have been successfully patented [D1].

These fundamental studies have also uncovered the mechanism of rearrangement reactions of protonated [A27] and deprotonated peptide ions [A28]. For example protonated Gly-Arg and Arg-Gly give identical tandem mass spectra (MS/MS) thereby precluding their sequence assignment. Density functional theory (DFT) calculations and further multistage mass spectrometry experiments suggest a mechanism which involves the formation of salt bridges for Gly-Arg and Arg-Gly, which then undergo ring closure, followed by ring opening, to form a mixed anhydride. Prevention of salt bridge formation through the use of methyl esters “switches off” this reaction and yields different MS/MS spectra, allowing sequence assignment.



Reaction #	Nucleophilic Neighbouring Group	Electrophilic Site / Leaving Group	Product Ion	Comments	Ref. #
1	Side chain	Backbone	non-sequence	R <sub>1</sub> = met, cys, lys, trp	[A17], [A23], [A29]
2	Side chain	Backbone	non-sequence	R <sub>1</sub> = cys & ser	[A16], [A20]
3	Backbone	Side chain	non-sequence	R <sub>3</sub> = ser & thr	[A19], [A20]
4	Backbone	Side chain	non-sequence	R <sub>2</sub> = ser & thr	[A19], [A20]
5	Backbone	Side chain	non-sequence	R <sub>2</sub> = met oxide & fixed charge met sulfonium	[A29]
6	Backbone	Backbone	sequence	key sequencing reaction to yield b and y ions	[A16], [A18]
7	Backbone	Backbone	non-sequence		[A18]
8	Side chain	Backbone	sequence	R <sub>3</sub> = asp via salt bridge	[A26]
9	Side chain	Backbone	sequence	R <sub>3</sub> = his	[A25]

**Scheme 1:** Examples of Neighbouring Group Participation Reactions in Peptide Ion Fragmentations (adapted from [E3]).

Using  $^{15}\text{N}$  isotopically labelled glycyl-glycine, MS/MS experiments reveal that the initial carbanion  $[\text{H}_2\text{NCH}_2\text{C}(\text{O})\text{NHCH}_2^-]$  formed via the collision induced loss of  $\text{CO}_2$  undergoes rearrangement to the nitrogen anion  $[\text{HNCH}_2\text{C}(\text{O})\text{NHCH}_3^-]$ . The latter ion is responsible for the subsequent fragmentation reactions. *Ab initio* calculations (at the MP2/6-31+G\* level of theory) reveal that this intramolecular rearrangement process proceeds via a six centered transition state with a modest activation energy (11.1 kcal mol $^{-1}$ ) and is overall exothermic by 3.2 kcal mol $^{-1}$ .

MS/MS studies have also been carried out to determine the fragmentation mechanisms of some important post-translational derivatives of amino acid residues found in peptides. Thus the side chain loss of MeSOH from methionine sulfoxide derivatives has been shown to be quite complex, and can involve either neighbouring group reactions or charge remote cis elimination reactions [A29]. The oxidized derivatives of tryptophan [A30, A31] have also been studied and show a rich gas phase chemistry.

The site of the charge, types of leaving groups, possibility of intramolecular processes etc, also play a role in the fragmentation reactions of protonated and deprotonated oligonucleotides [A32,A33] and models for sugars [A34]. Both protonated and deprotonated oligonucleotides fragment via loss of the nucleobase, and these "non-sequence" product ions can undergo further fragmentation to yield w-type or (a-B)-type "sequence" ions. The relative abundance of neutral nucleobase loss is dependant on the properties of the nucleobase and its position within the oligodeoxynucleotide sequence (5' > 3' > internal). For positive ions it follows the relative proton affinity (where  $\text{C} \approx \text{G} > \text{A} \gg \text{T}$ ) [A32], while for negative ions it follows the order  $\text{A} > \text{T} > \text{G} > \text{C}$  [A33].

**(5) Reactivity of radicals derived from peptides and oligonucleotides:** We have been interested in examining the gas phase radical chemistry of biomolecules for two main reasons: (i) from a fundamental perspective (recall from (2) that radicals can damage biomolecules); (ii) they are likely to exhibit complementary fragmentation reactions to their even electron counterparts, and thus might be used in analytical applications. In collaboration with Professor Bowie's group, neutralization-reionization was used to probe the  $[\text{M-H}]^\cdot$  radical of glycine [A35]. Collaborations with Associate Professor McFadyen have involved the use of Cu(II) ternary complexes,  $[\text{Cu}(\text{L})(\text{M})]^{2+}$  of peptides (M) and a variety of auxiliary ligands (L) to generate the radical cations,  $\text{M}^+$ , of simple peptides [A36-38]. The formation of  $\text{M}^+$  is in competition with a number of other reaction channels, and the yield of  $\text{M}^+$  is depends on both the structure of the peptide (M), as well as the auxiliary ligands [A38]. Complexes containing tridentate auxiliary ligands without acidic protons (e.g. terpy) and peptides with a basic residue (e.g. arginine) appear to give the highest yield of  $\text{M}^+$  [A38]. A number of gas phase fragmentation reactions unprecedented

for the even electron  $[M+H]^+$  ions have been discovered for peptide radical cations, including radical site migration reactions and side chain radical cleavage reactions [A36,A37]. The latter provides unique structural information, including the distinction between leucine and isoleucine residues in peptides [A36].

Radicals derived from models of DNA can also be generated in the gas phase using a number of techniques [A39-A42]. Silver (I) adenine polymers,  $[Ad_x+Ag_y-zH]^{(y-z)+}$  are readily formed via electrospray ionization. Both the charge and the stoichiometry of the  $[Ad_x+Ag_y-zH]^{(y-z)+}$  complexes plays a pivotal role in directing the types of fragmentation reactions observed [A39,A40]. The  $[Ad_2+Ag_2]^{2+}$  ion dissociate to  $[Ad+Ag]^+$  while  $[Ad_2+Ag_2-H]^+$  fragments via loss of neutral adenine to form the  $[Ad+Ag_2-H]^+$  ion. The latter ion undergoes a silver atom loss to form the  $[Ad+Ag-H]^+$  radical cation, which fragments quite differently to the even electron  $[Ad+Ag]^+$  ion [A40]. Results from two sabbaticals showed that: odd electron anions of deoxy-polyadenylates can be formed via ion-ion reactions between  $[M - nH]^-$  anions and  $Cl_3C^+$  and that these fragment differently to their even electron counterparts [A41]; electron capture dissociation of oligodeoxynucleotide dication yields radical cations which undergo a number of fragmentation reactions [A42].

**(6) Structure and reactivity of metallated peptides:** Metal ions play important roles in biology, and the advent of ESI allows their complexes with biological molecules to be examined in the gas phase. In collaboration with Associate Professor McFadyen, we have examined the fragmentation reactions of platinum-tridentate complexes of amino acids and peptides [A43,A44]. The types of fragmentation reactions depend on both the charge state, the nature of the amino acid or peptide and the structure of the tridentate ligand. In a collaboration with Professor Jarrold, ion-mobility mass spectrometry was used to examine how metal ions can influence the conformation of polyalanine peptides [A45].

**(7) Reactivity of non-covalent complexes:** Mass spectrometry (MS) has become an important analytical tool for the examination of non-covalent interactions of biological interest, due to the coupling of soft ionization techniques with the inherent four "S" advantages of MS: specificity, sensitivity, speed and stoichiometry. I have been interested in examining the fundamental reactivity of these complexes in the gas phase.

The simple proton bound dimer of sarcosine (Sar) and glycylglycine (GlyGly),  $[Sar+H+GlyGly]^+$ , exhibits interesting bimolecular reactivity in the gas phase [A46,A47]. H/D exchange of this dimer proceeds more readily than that of the monomer ions  $[Sar+H]^+$  and  $[GlyGly+H]^+$ , suggesting that the dimer offers opportunities for acid and base assistance in the H/D exchange process [A46]. Bases react with  $[Sar+H+GlyGly]^+$  via two main reaction channels: association and ligand switching [A47]. The association reaction



occurs more readily for the oxygen containing bases and those with a lower gas phase basicity. Molecular recognition was demonstrated for the ligand switching reactions, in which nitrogen containing bases with low dipole moments prefer to switch out sarcosine, while the oxygen containing bases with high dipole moments prefer to switch out glycylglycine.

The protonated homochiral octamer of serine exchanges all 33 of its labile hydrogens with  $\text{CH}_3\text{OD}$  and undergoes ligand-switching reactions with amines in a quadrupole ion trap mass spectrometer [A48]. The proton affinity of the amine is the key factor in determining the rate of ligand switching. Of particular interest is that strong bases undergo a rapid replacement in the first ligand-switching reaction, but the second one (replacement of a second serine with the amine) is too slow to observe. This result can be rationalized for an ionic structure of the  $(\text{Ser})_8\text{H}^+$  cluster, in which all but the protonated serine exist in a zwitterionic form ( $^+\text{H}_3\text{NCHRCO}_2^-$ ). Thus the unique protonated serine is able to undergo the exchange process with the amine to give the  $(\text{Ser})_7(\text{amine})\text{H}^+$  cluster, in which the charge is now effectively localized on the introduced amine. The remaining serines in the cluster maintain their zwitterionic form, rendering them unreactive towards further exchange with the amine. The chirality of the ligand was shown to play a minor role in exchange in the reactions of other clusters with the general structure  $(\text{Ser})_7(\text{amine})\text{H}^+$ .

We have also shown that trimethyl borate can be used as a gas phase “crosslinking reagent” for non-covalent anionic complexes of simple biomolecules which contain phosphate moieties [A49,A50]. This appears to be a general reaction, which operates for systems such as phosphoserine [A49] and nucleotides [A50].

The gas phase fragmentation reactions of proton bound oligosaccharide (S) -ligand (L) non-covalent complexes,  $[\text{S}+\text{H}+\text{L}]^+$  can be broadly classified into three main types: (1) simple dissociation into the individual monomers; (2) cleavage of the oligosaccharide to form B-type sequence ions; (3) cleavage of the ligand species [A51,A52]. The second type of reaction is particularly interesting, since it involves a novel ligand induced cleavage reactions of the glycosidic bond. Both the oligosaccharide and ligand were found to influence the type of reaction pathway observed, with reaction (2) being favoured for permethylated oligosaccharides (both  $\beta$ -cyclodextrins and linear sugars) and for bifunctional ligands, such as nucleobases.

**(8) Analytical applications:** I have been involved in a number of collaborations which utilized mass spectrometry to investigate the structures of natural products: post-doctoral research demonstrated that  $\beta$  crystallin is a component of the urea-insoluble protein

fraction [A53]; a novel strategy using stable isotope labelling, cross-linking and tandem mass spectrometry was used to examine protein-protein interactions in the interleukin-6 dimer [A54]; multistage mass spectrometry in conjunction with other spectroscopic techniques was used to structurally characterize the Aspergillicins A-E, five cyclic hexadepsipeptides from the marine-derived fungus *Aspergillus carneus* [A55].

### **(B) Inorganic and Organometallic Gas Phase Ion Chemistry:**

This broad area of research has focussed on fundamental gas phase ion chemistry of inorganic and organometallic systems. Key results in the following sub areas are now discussed:

**(1) Reactions of organosilicon, organophosphorus and organosulfur species:** Most of the studies were carried out when I was a postdoctoral fellow, working with Professors DePuy and Damrauer and Dr Bierbaum. A number of these studies involved examining the synthesis and reactivity of unusual, low valent silicon, phosphorus and sulfur ions such as  $\text{HSiS}^-$  and  $\text{HSiNH}^-$  [B1];  $\text{HSiO}^-$  [B2];  $\text{HP}_2^-$ ,  $\text{FP}_2^-$  and  $\text{HP}_2^+$  [B3];  $\text{HOS}^-$  [B4];  $\text{CH}_3\text{SO}^-$  and  $\text{CH}_3\text{SS}^-$  [B5]. By studying the thermochemistry of their reactions (e.g. proton transfer), the gas phase properties of related neutrals could be determined. For example, detailed studies on  $\text{HOS}^-$  yielded: its heat of formation; the electron affinity of the radical  $\text{HOS}^\cdot$ ; the gas phase acidity of  $\text{HOSH}$ ; the bond dissociation of  $\text{HOSH}$ . At Kansas State University we examined the reactions of nucleophiles with  $\text{PF}_3$  [B6] and dimethoxydisulfide and diethoxydisulfide [B7] in a flowing afterglow apparatus. The former proceed via a mechanism involving initial attack by the anion,  $\text{Nu}^-$ , at phosphorus to form an energized tetracoordinate anion intermediate,  $\text{NuPF}_3^-$ , which either undergoes collisional stabilization with helium, or undergoes fragmentation via loss of HF, if the original anion contains an acidic proton(s). In contrast, the reactions of nucleophiles with the dialkoxydisulfides, ROSSOR, are more complex and can occur via: cleavage of the sulfur-sulfur bond to form  $\text{ROS}^-$  ions; elimination to give  $\text{ROSS}^-$  ions; and attack at carbon to yield  $\text{ROSSO}^-$  ions. For some nucleophiles ( $\text{HA}^-$ ), anions of the type  $\text{HAS}^-$ ,  $\text{ROSA}^-$ , and  $\text{ROSSA}^-$  are also formed. Finally, the relative acidities of 14 sulfonic acids,  $\text{RSO}_3\text{H}$ , a class of "super acids" were determined via Cook's kinetic method [B8].

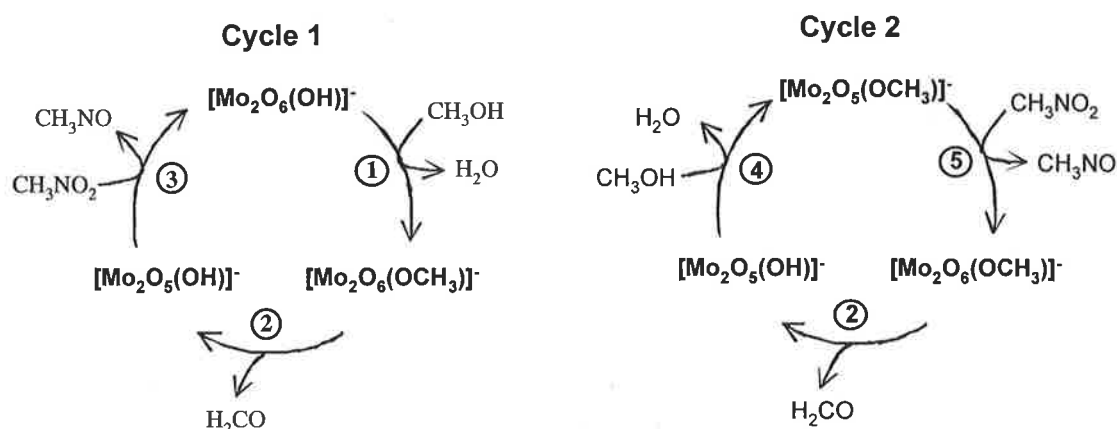
**(2) Gas phase coordination chemistry of platinum:** At Melbourne we have engaged in a collaborative program with Associate Professor McFadyen to examine the gas phase chemistry of platinum (II) complexes. We have shown that ESI/MS can be used to monitor the solution phase substitution products of complexes, such as  $[\text{Pt}(\text{dien})\text{Cl}]^+$  and  $[\text{Pt}(\text{Me}_3\text{dien})\text{Cl}]^+$  [B9]. Moreover, the  $[\text{Pt}(\text{dien})\text{X}]^{n+}$  ions, ( $n = 1$ , X=bromide, iodide, thiocyanate, cyanate, azide, nitrite and  $n = 2$ , X = pyridine) exhibit interesting fragmentation behaviour under CID conditions [B9-B12]. In most cases, the ligand is lost

as HX, giving rise to the coordinatively unsaturated  $[\text{Pt}(\text{dien})\text{-H}]^+$  ion. Notable exceptions include  $n = 1$ , where  $X = \text{N}_3^-$  and  $\text{NO}_2^-$ , which instead exhibit ligand fragmentation via loss of  $\text{N}_2$  and  $\text{NO}$  respectively to yield the novel platinum species  $[\text{Pt}(\text{dien})\text{N}]^+$  and  $[\text{Pt}(\text{dien})\text{O}]^+$ . Follow up studies have examined  $\text{N}_2$  loss from Pt bound azide systems [B10,B11] and have shown that the ligand loss channel is not as straightforward as originally thought [B12]. Thus deuterium labelling studies were used to uncover the source of protons associated with the ligand loss channel of  $\text{HX}^{(n-1)+}$  from  $[\text{Pt}(\text{dien})\text{X}]^{n+}$  ( $X = \text{Cl}, \text{Br}$  and  $\text{I}$  for  $n=1$  and  $X = \text{pyridine}$  for  $n=2$ ), and revealed that these protons originate from both the amino groups and the carbon backbone of the dien ligand. In some instances (e.g.  $X = \text{Br}$  and  $\text{I}$ ), the protons lost from the carbon backbone can be even more abundant than the protons lost from the amino groups. Labelling studies ( $^{15}\text{N}$  and deuterium labelling of the dien ligand) were also employed to examine further the loss of nitrogen from  $[\text{Pt}(\text{dien})\text{N}_3]^+$  and the subsequent fragmentation reactions of the  $[\text{Pt}(\text{dien})\text{N}]^+$  ion [B11]. Once again, the protons of both the amino group and the carbon backbone of the dien ligand are involved the loss of  $\text{NH}_3$  from  $[\text{Pt}(\text{dien})\text{N}]^+$ . These studies highlight the importance of using labelling to uncover the complexities of the CID fragmentation reactions of metal complexes. In addition to these unimolecular studies, a number of ion-molecule reactions of platinum complexes and their CID fragments have been examined. For example, the gas-phase substitution reactions of coordinatively saturated  $[\text{Pt}(\text{L}_3)\text{L}_a]^{2+}$  complexes ( $\text{L}_3 = \text{terpy}$  or dien) were shown to depend on both the ancillary ligand ( $\text{L}_3$ ), as well as the leaving group ( $\text{L}_a$ ) [B12].  $[\text{Pt}(\text{terpy})\text{L}_a]^{2+}$  complexes undergo substitution reactions, with a faster rate when  $\text{L}_a$  is a good leaving group, while  $[\text{Pt}(\text{dien})\text{L}_a]^{2+}$  complex undergoes a proton transfer reaction.

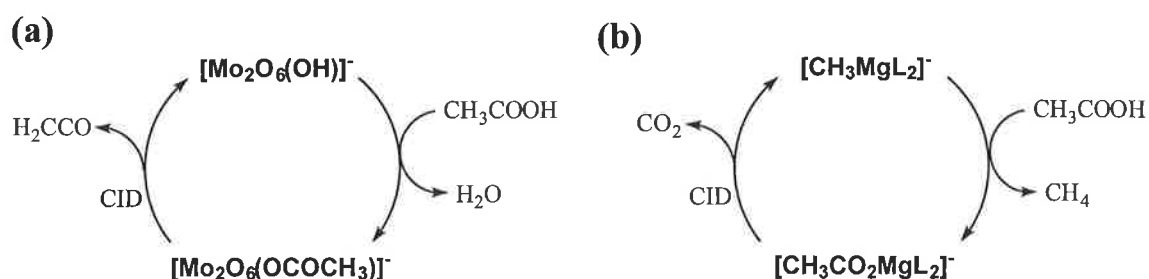
Our interest in the fundamental chemistry of platinum complexes prompted us to examine the thermochemistry of these systems [B13-B15]. Attempts to use the kinetic method to correlate the competition between pyridine ligand loss in the doubly and singly charged ions of complexes consisting of platinum(ethylenediamine) coordinated to 2 different substituted pyridines failed [B13]. Collision induced dissociation of  $[\text{Pt}(\text{en})\text{Py}_1\text{Py}_2]^{2+}$  (where  $\text{Py}_1 =$  one of ten different substituted pyridines and  $\text{Py}_2 =$  pyridine) results in loss of the protonated pyridines, to yield the singly charged platinum ions  $[\text{Pt}(\text{en})\text{Py}_1\text{-H}]^+$  and  $[\text{Pt}(\text{en})\text{Py}_2\text{-H}]^+$ . In contrast, fragmentation of  $[\text{Pt}(\text{en})\text{Py}_1\text{Py}_2\text{-H}]^+$  results in neutral pyridine loss, to yield the ions  $[\text{Pt}(\text{en})\text{Py}_1\text{-H}]^+$  and  $[\text{Pt}(\text{en})\text{Py}_2\text{-H}]^+$ . In the latter case, the correlation between relative losses of each pyridine compared to their gas phase proton affinities is poor. Collaborations with Professor Armentrout resulted in the determination of the sequential bond energies of  $\text{Pt}^+(\text{NH}_3)_x$  ( $x = 1 - 4$ ) via collision-induced dissociation with Xe, using guided-ion beam tandem mass spectrometry [B14]. The same technique was used to examine the reactions of  $\text{Pt}^+$  and  $\text{PtCl}^+$  with  $\text{Cl}_2$ , the ligand exchange

reactions of  $\text{PtCl}^+$  and  $\text{PtCl}_2^+$  with CO, and the CID reactions of  $\text{PtCl}^+$ ,  $\text{PtCl}_2^+$ , and  $\text{PtClCO}^+$ . These reactions yielded bond dissociation energies for  $\text{Pt}^+-\text{Cl}$  and  $\text{ClPt}^+-\text{Cl}$ .

**(3) Insights into catalysis by transition metal oxides and peroxides:** In collaboration with Professor Wedd, we have used multistage mass spectrometry experiments in a quadrupole ion trap, combined with isotope labelling studies, to examine the gas phase chemistry of group VI metal-oxo and peroxy systems [B16-B19]. In addition, photoelectron spectroscopy was used in collaborations with Professor Wang to examine the electronic structures of related systems [B20,B21]. We have uncovered novel gas phase catalytic cycles for the: oxidation of alcohols via an anionic dimolybdate center (Figure 2) [B16,B17]; and the dehydration of acetic acid (Figure 3a) [B18].



**Figure 2:** Gas phase catalytic cycles for the oxidation of methanol to formaldehyde. Reaction 2 links  $[\text{Mo}_2\text{O}_6(\text{OCH}_3)]^-$  and  $[\text{Mo}_2\text{O}_5(\text{OH})]^-$  and appears in both cycles. Cycles 1 and 2 differ in the sequence of reaction with  $\text{CH}_3\text{NO}_2$  and  $\text{CH}_3\text{OH}$



**Figure 3:** Gas phase catalytic cycles for the metal mediated: (a) dehydration of acetic acid; (b) decarboxylation of acetic acid.

The oxidation of primary and secondary alcohols to aldehydes involves two gas phase catalytic cycles (Cycles 1 and 2 in Figure 2), mediated by a binuclear dimolybdate center  $[\text{Mo}_2\text{O}_6(\text{OCH}_3)]^-$ , acting as the catalyst. The first cycle proceeds via three steps: (1) reaction of  $[\text{Mo}_2\text{O}_6(\text{OH})]^-$  with alcohol  $\text{R}_2\text{HCOH}$  and elimination of water to form  $[\text{Mo}_2\text{O}_6(\text{OCHR}_2)]^-$ ; (2) oxidation of the alkoxo ligand and its elimination as aldehyde in the rate-determining step; and (3) regeneration of the catalyst via oxidation by nitromethane. Step (2) does not occur at room temperature and requires the use of collisional activation to proceed. The second cycle is similar, but differs in the order of reaction with alcohol and nitromethane. The nature of each of these reactions was probed by kinetic measurements and by variation of the substrate alcohols (structure and isotope labelling). The role of the binuclear molybdenum center was assessed by examination of the relative reactivities of the mononuclear  $[\text{MO}_3(\text{OH})]^-$  and binuclear  $[\text{M}_2\text{O}_6(\text{OH})]^-$  ions ( $\text{M} = \text{Cr}, \text{Mo}, \text{W}$ ). The molybdenum and tungsten binuclear centers  $[\text{M}_2\text{O}_6(\text{OH})]^-$  ( $\text{M} = \text{Mo}, \text{W}$ ) were reactive towards alcohol, but the chromium center  $[\text{Cr}_2\text{O}_6(\text{OH})]^-$  was not. This is consistent with the expected order of basicity of the hydroxo ligand in these species. The chromium and molybdenum centers  $[\text{M}_2\text{O}_6(\text{OCHR}_2)]^-$  ( $\text{M} = \text{Cr}, \text{Mo}$ ) oxidized the alkoxo ligand to aldehyde, while the tungsten center  $[\text{W}_2\text{O}_6(\text{OCHR}_2)]^-$  did not, instead preferring the non-redox elimination of alkene. This is consistent with the expected order of oxidizing power of the anions. Each of the mononuclear anions  $[\text{MO}_3(\text{OH})]^-$  ( $\text{M} = \text{Cr}, \text{Mo}, \text{W}$ ) was inert to reaction with methanol, highlighting the importance of the second  $\text{MoO}_3$  unit in these catalytic cycles. Only the dimolybdate center has the right mix of properties that allows it to participate in *each* of the three steps of the two catalytic cycles. The three reactions of these cycles are equivalent to the three essential steps proposed to occur in the industrial oxidation of gaseous methanol to formaldehyde at 300-400 °C over solid state catalysts based upon molybdenum(VI)-trioxide. In contrast, the catalytic dehydration of acetic acid (Figure 3a) is a two step process that is less sensitive towards the structure of the catalyst, working for both molybdenum and tungsten mononuclear and binuclear anions.

The oxidizing effects of oxo versus peroxo ligands were compared by examining the gas phase oxidation of alkoxo ligands in bis(peroxo)  $[\text{MO}(\text{O}_2)_2(\text{OR})]^-$  and trisoxo  $[\text{MO}_3(\text{OR})]^-$  anions ( $\text{M} = \text{Cr}, \text{Mo}, \text{W}$ ) **[B19]**. The molybdate and tungstate anions  $[\text{MO}(\text{O}_2)_2(\text{OR})]^-$  underwent parallel elimination of aldehyde (ketone) and dioxygen while the equivalent chromate underwent loss of dioxygen only. The peroxo ligands were the source of oxidizing equivalents in both reactions. For each alkoxo ligand, the total yield of aldehyde for the tungstate system exceeded that for the molybdate system. Collisional activation of  $[\text{MO}_3(\text{OMe})]^-$  led to clean elimination of formaldehyde with the metal center supplying the oxidizing equivalents. For larger alkoxo ligands, only the chromate center eliminated aldehyde, while the molybdate and tungstate centers underwent clean loss of alkene. Threshold activation voltages indicated that the peroxo ligands of  $[\text{WO}(\text{O}_2)_2(\text{OMe})]^-$

are more oxidizing than the tungstate center of  $[\text{WO}_3(\text{OMe})]^-$ . Deuterium and  $^{18}\text{O}$  isotope tracing experiments were consistent with a formal hydride transfer mechanism operating for oxidation of alkoxo ligand in each system.

**(4) Synthesis and reactivity of organometallics:** Recently we have been interested in using CID to synthesise novel organometallic species in the gas phase [B22-B25]. Decarboxylation of metal acetates appears to be a general way of synthesizing organometallic “ate” species, some of which are related to textbook organometallic species, used in organic synthesis (e.g. Grignard and Gilman reagents). These studies highlight the powerful multistage mass spectrometry capabilities of the ion trap. For example, two stages of CID and one ion-molecule reaction event (a  $\text{MS}^4$  experiment) are required to synthesize and study the reactions of  $(\text{CH}_3)_2\text{M}^-$  ( $\text{M} = \text{Cu}$  and  $\text{Ag}$ ) with methyl iodide in the gas phase [B23]. While the dimethylcuprate ion ( $\text{M} = \text{Cu}$ ) reacts with  $\text{CH}_3\text{I}$  via C-C bond cross coupling, its silver congener is unreactive. The experimental results are consistent with MP2/6-31++G\*\* *ab initio* calculations, which reveal that the preferred mechanism for Cu involves the formation of a T shaped Cu transition state.

The organomagnesates  $[\text{CH}_3\text{MgL}_2]^-$  ( $\text{L} = \text{Cl}$  and  $= \text{O}_2\text{CCH}_3$ ) exhibit some of the reactivity of Grignard reagents, reacting with neutral species containing an acidic proton (HX) via addition with concomitant elimination of methane to form  $[\text{XMgL}_2]^-$  ions [B24]. Kinetic measurements, combined with DFT calculations, revealed reduced reactivity of  $[\text{CH}_3\text{Mg}(\text{O}_2\text{CCH}_3)_2]^-$  towards water, caused by the bidentate binding mode of acetate, which induces overcrowding of the Mg coordination sphere. The  $[\text{CH}_3\text{MgL}_2]^-$  ions reacted with aldehydes containing enolizable protons via enolization, rather than the Grignard reaction. This is consistent with DFT calculations on the competition between enolization and the Grignard reaction for  $[\text{CH}_3\text{MgCl}_2]^-$  ions reacting with acetaldehyde, which suggest that while the latter has a smaller barrier, it is entropically disfavoured. Interestingly, the  $[\text{CH}_3\text{MgL}_2]^-$  ions complete a catalytic cycle for the decarboxylation of acetic acid (Figure 3b). Thus we have discovered two different metal catalysts which selectively activate acetic acid to decompose via dehydration (Figure 3a) or decarboxylation (Figure 3a).

Organometallic species can also be synthesized via indirect routes. For example, the  $\text{Ag}_4\text{H}^+$  cluster is formed via CID of silver-amino acid clusters and reacts selectively with allylbromide to form initially the  $\text{Ag}_4\text{Br}^+$  cluster. Subsequent reactions of this ion with allylbromide yield the  $\text{Ag}_4\text{Br}_2(\text{allyl})^+$  species, which further reacts to form  $\text{Ag}(\text{C}_6\text{H}_{10})^+$  and the neutral cluster  $\text{Ag}_3\text{Br}_3$ . Comparison of the energy resolved CID spectrum of the  $\text{Ag}(\text{C}_6\text{H}_{10})^+$  ion with ions of “authentic” structures, reveal that the  $\text{C}_6\text{H}_{10}$  species formed in the ion-molecule reactions of the  $\text{Ag}_4\text{H}^+$  cluster with allylbromide corresponds to 1,5 hexadiene [B25].

### (C) Miscellaneous Organic Gas Phase Ion Chemistry

Many of the areas discussed above in sections (A) and (B) have important connections to organic chemistry. In this section various other papers, relevant to gas phase organic chemistry, are described, including those which examine: thermochemistry; mechanisms of ion-molecule reactions; and the formation of unusual species and reactive intermediates. In my post-doctoral research, I determined: the gas phase acidities of some hindered amines and the reactions of their conjugate bases [C1]; solvent and substrate deuterium kinetic isotope effects for the gas-phase  $S_N2$  reactions of fluoride and its monohydrated cluster with methyl halides [C2]. More recently, we have examined the mechanisms of substitution reactions at  $sp^2$  hybridised carbon atoms [C3,C4]. We have shown that the thermoneutral identity exchange reactions between N-acylpyridinium ions and pyridines can occur in the gas phase. The nature of the acyl group plays a crucial role, with the bimolecular rates following the order acetyl > benzoyl > N,N-dimethylaminocarbonyl. The experimental results correlate with *ab initio* calculations on a simple model system  $RC(O)NH_3^+ + NH_3$ , which also demonstrates that these are "S<sub>N</sub>2 like" processes. In contrast, aryl diazonium ions do not undergo nucleophilic substitution reactions in the gas phase [C4]. They do, however, readily fragment via  $N_2$  loss to form highly reactive aryl cations, which undergo a number of reactions with nucleophiles. The gas phase reactions of anions,  $R^-$ , with nitrous oxide,  $N_2O$ , have been widely examined by the DePuy group. As a post-doctoral researcher, I discovered a way of synthesizing the proposed adduct from attack at the terminal nitrogen,  $RN_2O^-$ . Under CID, these were shown to give similar products to those from direct reactions of  $H^-$  and  $N_2O$  [C5] and other carbanions with  $N_2O$  [C6]. In a collaboration with Professor Bowie, we examined the gas phase Cannizzaro disproportionation reactions of benzaldehyde and pivaldehyde [C7]. More recently, we discovered a new rearrangement reaction of the radical anion of 1,2-dicyanoethylenedithiolate, which results in the formation of the heterocumulene anion  $SCCCN^-$  by a cyano migration [C8].

#### Statement of Candidate's Contribution towards the Authorship of each Publication.

The research presented in this thesis has mainly been carried out at Kansas State University and the University of Melbourne with the collaboration of research students and assistants, who have contributed to the bulk of the practical aspects of this work. I have been solely responsible for the supervision and the direction of the research, except for collaborations with other research groups, as noted elsewhere. As required by Section 3(c) of the Academic Program Rules for the degree of Doctor of Science at the University of Adelaide, in the list of publications section, I have estimated my contributions to the intellectual aspects of the work. I have also identified the role of the other authors (e.g. PhD student, collaborator, etc.).

## **Statement**

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference is made in the text.

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Richard A. J. O'Hair, Ph.D., FRACI

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December 2004



*"The scientific paper is a kind of fraud. The neat format 'Introduction' followed by 'Methods' then 'Results' and finally 'Discussion' bears no relation to the way scientists actually work. While the final results must stand up to cold and objective scrutiny, the process of achieving them rarely takes a form of the calm and logical progression suggested by the telling. Purging events of all human emotion, the formal impersonal style totally fails to indicate who actually did what and why. If the effort was a collaborative one, a whole team of widely differing individuals condenses into a faceless, characterless, Delphic oracle of science. The technicians disappear completely. So do imagination and chance, confusion and failure and the vital conversations in the coffee room and thoughts in the bath. It is, perhaps, hardly surprising that scientists are felt to lack a certain human touch."*

**P.B. Medawar (quoted by L. Wolpert and A. Richards in 'A Passion for Science', Oxford University Press, 1988, page 2).**

## List of Publications

### Publications (A): Gas Phase Ion-Chemistry and Mass Spectrometry of Biomolecules

- (A1) O'Hair, R. A. J.; Bowie, J. H.; Gronert, S., "Gas Phase Acidities of the  $\alpha$  Amino Acids", *Int. J. Mass Spectrom. Ion Proc.*, **1992**, *117*, 23-36. "Gas Phase Ion Chemistry of Biomolecules. Part 1" (O'Hair 80% principal author; Bowie: Post-Doctoral Supervisor; Gronert: San Francisco State University collaborator)
- (A2) O'Hair, R. A. J.; Gronert, S.; Williams, T. D., "How Does Isotopic Substitution Affect the Gas-Phase Proton Affinity of Glycine? A Combined Experimental and *Ab Initio* Study", *Org. Mass Spectrom.*, **1994**, *29*, 151-152. "Gas Phase Ion Chemistry of Biomolecules. Part 2" (O'Hair 80% principal author; Gronert: San Francisco State University collaborator; Williams: University of Kansas collaborator)
- (A3) Gronert, S.; O'Hair, R. A. J., "*Ab Initio* Studies of Amino Acid Conformations 1. The Conformers of Alanine, Serine, and Cysteine", *J. Am. Chem. Soc.*, **1995**, *117*, 2071-2081. (O'Hair 10%; Gronert: principal author and San Francisco State University collaborator)
- (A4) O'Hair, R. A. J.; Freitas, M. A.; Gronert, S.; Schmidt, J. A. R.; Williams, T. D., "Concerning the Regioselectivity of Gas Phase Reactions of Glycine with Electrophiles. The Cases of the Dimethylchlorinium Ion and the Methoxymethyl Cation.", *J. Org. Chem.*, **1995**, *60*, 1990-1998. "Gas Phase Ion Chemistry of Biomolecules. Part 3" (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Gronert: San Francisco State University collaborator; Schmidt: undergraduate student; Williams: University of Kansas collaborator)
- (A5) Freitas, M. A. ; O'Hair, R. A. J.; Williams, T. D., "Gas Phase Reactions of Cysteine with Charged Electrophiles: Regioselectivities of the Dimethylchlorinium Ion and the Methoxymethyl Cation.", *J. Org. Chem.*, **1997**, *62*, 6112-6120. "Gas Phase Ion Chemistry of Biomolecules. Part 7" (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Williams: University of Kansas collaborator)
- (A6) Freitas, M. A. ; O'Hair, R. A. J., "Characterization of an Ambident Electrophile: The Gas Phase Reactivity of the Methoxymethyl Cation.", *Int. J. Mass Spectrom. Ion Proc.*, **1998**, *175*, 107-122. (O'Hair 80% principal author and research supervisor; Freitas: PhD student)
- (A7) O'Hair, R. A. J.; Freitas, M. A.; Williams, T. D., "Gas Phase Reactions of the Cyclic Ethylene Halonium Ions  $(\text{CH}_2)_2\text{X}^+$  (X = Cl, Br) with Glycine.", *J. Org. Chem.*, **1996**, *61*, 2374-2382. "Gas Phase Ion Chemistry of Biomolecules. Part 5"

- (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Williams: University of Kansas collaborator)
- (A8) Freitas, M. A. ; O'Hair, R. A. J.; Schmidt, J. A. R.; Tichy, S. E.; Plashko, B. E.; Williams, T. D., "Gas Phase Reactions of Glycine, Alanine, Valine and Their N-Methyl Derivatives with the Nitrosonium Ion, NO<sup>+</sup>." , *J. Mass Spectrom.*, **1996**, *31*, 1086-1092. "Gas Phase Ion Chemistry of Biomolecules. Part 6" (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Schmidt: undergraduate student; Tichy: PhD student; Plashko: Kansas State University collaborator; Williams: University of Kansas collaborator)
- (A9) O'Hair, R. A. J.; Freitas, M. A.; Schmidt, J. A. R.; Hatley, M. E. Williams, T. D., "Gas- Phase Methylation of the 2-Hydroxypyridine/2-Pyridone System by the Dimethylchlorinium Ion." , *Eur. Mass Spectrom.*, **1995**, *1*, 457-463. "Gas Phase Ion Chemistry of Biomolecules. Part 4" (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Schmidt: undergraduate student; Hatley: undergraduate student; Williams: University of Kansas collaborator)
- (A10) Freitas, M. A. ; O'Hair, R. A. J.; Dua, S.; Bowie, J.H., "The Methoxymethyl Cation Cleaves Peptide Bonds in the Gas Phase." , *Chem. Commun.* , **1997**, 1409-1410. "Gas Phase Ion Chemistry of Biomolecules. Part 8" (O'Hair 80% principal author and research supervisor; Freitas: PhD student; Dua and Bowie: University of Adelaide collaborators)
- (A11) O'Hair, R. A. J.; Gronert, S., "Ab Initio Insights Into Amide Bond Cleavage Reactions of Formamide with Substituted Methyl Cations XCH<sub>2</sub><sup>+</sup> (X = OH, F & Cl)." , *Int. J. Mass Spectrom.*, **2000**, *195*, 303-307. (O'Hair 80% principal author; Gronert: San Francisco State University collaborator)
- (A12) O'Hair, R. A. J.; Androustopoulos, N. K.; Reid, G.E., "Do Amines React with Protonated Peptides in the Gas Phase via Transacylation Reactions to Induce Peptide Bond Cleavage?" , *Rapid Commun. Mass Spectrom.*, **2000**, *14*, 1707-1716. "Gas Phase Ion Chemistry of Biomolecules. Part 26" (O'Hair 80% principal author and research supervisor; Androustopoulos: PhD student; Reid: honours student)
- (A13) Reid, G. E.; Tichy, S. E. ; Pérez, J.; O'Hair, R. A. J.; Simpson, R. J.; Kenttämaa H. I., "N-terminal Derivatization and Fragmentation of Neutral Peptides via Ion-Molecule Reactions with Acylium Ions: Towards Gas-Phase Edman Degradation?" *J. Am. Chem. Soc.*, **2001**, *123*, 1184-1192. (O'Hair joint research supervisor; Reid and Tichy: PhD students and joint principal authors; Pérez and Kenttämaa: Purdue University collaborators; Simpson: Ludwig Institute for Cancer Research collaborator)

- (A14) O'Hair, R. A. J.; Reid, G.E., "Derivatization of Protonated Peptides via Gas Phase Ion-molecule Reactions with Acetone" *J. Am. Soc. Mass Spectrom.*, **2000**, *11*, 244-256. "Gas Phase Ion Chemistry of Biomolecules. Part 19" (O'Hair 60% principal author and research supervisor; Reid: PhD student)
- (A15) O'Hair, R. A. J.; McLuckey, S.A., "Trimethylsilyl Derivatization of Nucleic Acid Anions in the Gas Phase.", *Int. J. Mass Spectrom. Ion Proc.*, **1997**, *162*, 183-202. (O'Hair 80%; McLuckey: principal author and Oak Ridge National Laboratory collaborator)
- (A16) Reid, G. E.; Simpson, R. J.; O'Hair, R. A. J., "A Mass Spectrometric and *ab initio* Study of the Pathways for Dehydration of Simple Glycine and Cysteine Containing Peptide  $[M+H]^+$  Ions.", *J. Am. Soc. Mass Spectrom.*, **1998**, *9*, 945-956. "Gas Phase Ion Chemistry of Biomolecules. Part 10" (O'Hair 80% principal author and joint research supervisor; Reid: honours student; Simpson: Ludwig Institute for Cancer Research collaborator)
- (A17) O'Hair, R. A. J.; Styles, M.L.; Reid, G.E., "Role of the Sulfhydryl Group on the Gas Phase Fragmentation Reactions of Protonated Cysteine and Cysteine Containing Peptides.", *J. Am. Soc. Mass Spectrom.*, **1998**, *9*, 1275-1284. "Gas Phase Ion Chemistry of Biomolecules. Part 13" (O'Hair 80% principal author and joint research supervisor; Styles: PhD student; Reid: honours student)
- (A18) Reid, G.E.; Simpson, R.J.; O'Hair, R. A. J., "Probing the Fragmentation Reactions of Protonated Glycine Oligomers via Multistage Mass Spectrometry and Gas Phase H/D Exchange in a Modified Ion Trap.", *Int. J. Mass Spectrom.*, **1999**, *190/191*, 209-230. "Gas Phase Ion Chemistry of Biomolecules. Part 17" (O'Hair 70% principal author and joint research supervisor; Reid: PhD student; Simpson: Ludwig Institute for Cancer Research collaborator)
- (A19) O'Hair, R. A. J.; Reid, G.E., "Does Side Chain Water Loss from Protonated Threonine Yield N-Protonated Dehydroamino-2-butyric acid?", *Rapid Commun. Mass Spectrom.*, **1998**, *12*, 999-1002. "Gas Phase Ion Chemistry of Biomolecules. Part 14" (O'Hair 70% principal author and research supervisor; Reid: PhD student)
- (A20) Reid, G.E.; Simpson, R.J.; O'Hair, R. A. J., "Leaving Group and Gas Phase Neighbouring Group Effects in the Side Chain Losses From Protonated Serine and its Derivatives.", *J. Am. Soc. Mass Spectrom.*, **2000**, *11*, 1047-1060. "Gas Phase Ion Chemistry of Biomolecules. Part 25" (O'Hair 50% principal author and joint research supervisor; Reid: PhD student; Simpson: Ludwig Institute for Cancer Research collaborator)
- (A21) O'Hair, R. A. J.; Broughton, P. S.; Styles, M. L.; Frink, B. T.; Hadad, C. M., "The Fragmentation Pathways of Protonated Glycine. A Computational Study", *J. Am. Soc. Mass Spectrom.*, **2000**, *11*, 687-696. "Gas Phase Ion Chemistry of

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- (A22) O'Hair, R. A. J.; Reid, G.E., "The Search for Stable Gas Phase  $b_1$  Ions Derived from Aliphatic Amino Acids: A Combined Experimental and *Ab Initio* Study.", *Rapid Commun. Mass Spectrom.*, **2000**, *14*, 1220-1225. "Gas Phase Ion Chemistry of Biomolecules. Part 24" (O'Hair 60% principal author and research supervisor; Reid: honours student)
- (A23) Lioe, H.; O'Hair, R. A. J.; Reid, G.E. "Gas-Phase Reactions of Protonated Tryptophan.", *J. Am. Soc. Mass Spectrom.*, **2004**, *15*, 65-76. "Gas Phase Ion Chemistry of Biomolecules. Part 37" (O'Hair 50% joint principal author and joint research supervisor; Lioe: PhD student; Reid: joint principal author and Ludwig Institute for Cancer Research collaborator)
- (A24) Farrugia, J.M. ; O'Hair, R. A. J. ; Reid, G. E., "Do all  $b_2$  ions have Oxazolone Structures? Results from Multistage Mass Spectrometry and *ab initio* Studies on Protonated N-Acyl Amino Acid Methyl Ester Model Systems.", *Int. J. Mass Spectrom.*, **2001**, *210-211*, 71-87. "Gas Phase Ion Chemistry of Biomolecules. Part 28" (O'Hair 80% principal author and research supervisor; Farrugia: honours student; Reid: PhD student)
- (A25) Farrugia, J.M.; Taverner, T.; O'Hair, R. A. J. "Side Chain Involvement in the Fragmentation Reactions of Protonated Histidine and its Peptides.", *Int. J. Mass Spectrom.*, **2001**, *209*, 99-112. "Gas Phase Ion Chemistry of Biomolecules. Part 30" (O'Hair 80% principal author and research supervisor; Farrugia: honours student; Taverner: undergraduate student)
- (A26) Kapp, E. A.; Schütz, F.; Reid, G. E.; Eddes, J.S.; Moritz, R. L.; O'Hair, R. A. J.; Speed T. P.; Simpson, R. J. "Mining a Tandem Mass Spectrometry Database to Determine the Trends and Global Factors Influencing Peptide Fragmentation", *Anal. Chem.*, **2003**, *75*, 6251-6264. (O'Hair 10%; Simpson: principal author; Kapp, Schütz, Reid, Eddes, Moritz, Speed: Ludwig Institute for Cancer Research collaborators)
- (A27) Farrugia, J.M.; O'Hair, R. A. J. " Involvement of Salt Bridges in a Novel Gas Phase Rearrangement of Protonated Argine Containing Dipeptides which Precedes Fragmentation.", *Int. J. Mass Spectrom.*, (invited contribution to Professor Beauchamp Honour Issue) **2003**, *222*, 229-242. "Gas Phase Ion Chemistry of Biomolecules. Part 32" (O'Hair 80% principal author and research supervisor; Farrugia: honours student)

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- (A29) O'Hair, R. A. J.; Reid, G.E., "Neighboring Group Versus Cis Elimination Mechanisms for Side Chain Loss from Protonated Methionine, Methionine Sulfoxide and Their Peptides.", *Eur. Mass Spectrom.*, **1999**, *5*, 325–334. "Gas Phase Ion Chemistry of Biomolecules. Part 21" (O'Hair 60% principal author and research supervisor; Reid: PhD student)
- (A30) Vazquez, S.; Truscott, R. J. W.; O'Hair, R. A. J.; Weimann, A.; Sheil, M. M., "A Study of Kynurenine Fragmentation using Electrospray Tandem Mass Spectrometry.", *J. Am. Soc. Mass Spectrom.*, **2001**, *12*, 786-794. (O'Hair 10%; Sheil: principal author; Vazquez, Truscott, and Weimann University of Wollongong collaborators)
- (A31) Lioe, H.; O'Hair, R. A. J.; Reid, G.E., "A Mass Spectrometric and Molecular Orbital study of H<sub>2</sub>O loss from Protonated Tryptophan and Oxidized Tryptophan derivatives.", *Rapid Commun. Mass Spectrom.*, **2004**, *18*, 978–988. "Gas Phase Ion Chemistry of Biomolecules. Part 41 O'Hair 50% joint principal author and joint research supervisor; Lioe: PhD student; Reid: joint principal author and Ludwig Institute for Cancer Research collaborator)
- (A32) Vrkic, A. K.; O'Hair, R. A. J.; Foote, S.; Reid, G.E., "Fragmentation Reactions of All 64 Protonated Trimer Oligonucleotides and 16 Mixed Base Tetramer Oligonucleotides via Tandem Mass Spectrometry in an Ion Trap." *Int. J. Mass Spectrom.*, **2000**, *194*, 145-164. "Gas Phase Ion Chemistry of Biomolecules. Part 18" (O'Hair 80% principal author and research supervisor; Vrkic: Honours student; Reid: PhD student; Foote: Walter and Eliza Hall Institute for Medical Research collaborator)
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- (A34) Dua, S.; O'Hair, R. A. J.; Bowie, J. H.; Hayes, R. N., "The Negative Ion Mass Spectra of Deprotonated Carbohydrates. Part 1. The Basic Hydroxymethyl-substituted Ring Systems", *J. Chem. Soc. Perkin Trans. 2*, **1992**, 1151-1157. (O'Hair, 30% Postdoctoral researcher; Dua: University of Adelaide collaborator;

- Bowie principal author and research supervisor; Hayes: University of Nebraska collaborator)
- (A35) O'Hair, R. A. J.; Blanksby, S.; Styles, M. L.; Bowie, J.H., "Characterization of [M - H] Cations, Radicals and Anions of Glycine in the Gas Phase: A Combined Experimental and Ab Initio Study", *Int. J. Mass Spectrom.*, **1999**, 182/183, 203-211. "Gas Phase Ion Chemistry of Biomolecules. Part 16" (O'Hair 80% principal author and research supervisor; Styles: PhD student; Blanksby and Bowie: University of Adelaide collaborators)
- (A36) Wee, S.; O'Hair, R. A. J. ; McFadyen, W.D., "Side Chain Radical Losses from Radical Cations Allows Distinction of Leucine and Isoleucine Residues in the Isomeric Peptides Gly-XXX-Arg..", *Rapid Commun. Mass Spectrom.*, **2002**, 16, 884-890. "Gas Phase Ion Chemistry of Biomolecules. Part 31" (O'Hair 80% principal author and joint research supervisor; Wee: PhD student; McFadyen: joint research supervisor)
- (A37) Wee, S.; O'Hair, R. A. J.; McFadyen, W.D., "Comparing the Gas Phase Fragmentation Reactions of Protonated and Radical Cations of the Tripeptides GXR.", *Int. J. Mass Spectrom.*, (invited contribution to Professor Marshall Honour Issue), **2004**, 234, 101-122. "Gas Phase Ion Chemistry of Biomolecules. Part 40" (O'Hair 60% joint principal author and joint research supervisor; Wee: PhD student; McFadyen: joint principal author and joint research supervisor)
- (A38) Barlow, C.K.; Wee, S.; McFadyen, W.D.; O'Hair, R. A. J., "Designing Copper(II) Ternary Complexes to Generate Radical Cations of Peptides in the Gas Phase: Role of the Auxiliary Ligand.", *Dalton Trans.*, **2004**, 3199-3204. "Gas Phase Ion Chemistry of Biomolecules. Part 43" (O'Hair 50% joint principal author and joint research supervisor; Barlow and Wee: PhD students; McFadyen: joint principal author and joint research supervisor)
- (A39) Vrkic, A. K.; Taverner, T.; O'Hair, R. A. J. "Mapping Charged Silver (I) Adenine Polymers,  $[xAd+yAg-zH]^{(y-z)+}$ , via Electrospray Ionization Tandem Mass Spectrometry Experiments.", *Dalton Trans.*, **2002**, 4024-4034. "Gas Phase Ion Chemistry of Biomolecules. Part 33" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student; Taverner: undergraduate student)
- (A40) Vrkic, A. K.; Taverner, T.; James, P. F.; O'Hair, R. A. J. " Gas Phase Ion Chemistry of Charged Silver (I) Adenine Ions via Multistage Mass Spectrometry Experiments and DFT Calculations.", *Dalton Trans.*, **2004**, 197-208. "Gas Phase Ion Chemistry of Biomolecules. Part 38" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student; Taverner and James: undergraduate students)

- (A41) McLuckey, S.A.; Stephenson, J. L.; O'Hair, R. A. J., "Decompositions of Odd- and Even-Electron Anions Derived from Deoxy-Polyadenylates.", *J. Am. Soc. Mass Spectrom.*, **1997**, *8*, 148-154. (O'Hair: 30%; McLuckey: principal author with Stephenson ORNL collaborator)
- (A42) Håkansson, K.; Hudgins, R.R.; Marshall A.G.; O'Hair, R. A. J. "Electron Capture Dissociation and Infrared Multiphoton Dissociation of Oligodeoxynucleotide Dications ", *J. Am. Soc. Mass Spectrom.*, **2003**, *14*, 23-41. (O'Hair 40% joint principal author; Håkansson and Hudgins Florida State University collaborators; Marshall: joint principal author and Florida State University collaborator)
- (A43) O'Hair, R. A. J., "Formation and Fragmentation Reactions of Platinum-terpyridine Complexes of Glycine, Cysteine and Their Methyl Derivatives Via Electrospray Ionization Mass Spectrometry.", *Eur. Mass Spectrom.*, **1997**, *3*, 390–395. "Gas Phase Ion Chemistry of Biomolecules. Part 9" (O'Hair 100%)
- (A44) Styles, M. L. ; O'Hair, R. A. J. ; McFadyen, W. D., " Evaluating the role of the ligand in the fragmentation reactions of platinum(II) complexes of aliphatic dipeptides. Electrospray ionization tandem mass spectrometry of  $[\text{Pt}(\text{L}_3)\text{M}]^{2+}$  and  $[\text{Pt}(\text{L}_3)\text{M} - \text{H}]^+$  ions [ $\text{L}_3 = (\text{H}_3\text{N})_3$ , diethylenetriamine and terpyridine;  $\text{M} = \text{gly-gly}$ ,  $\text{ala-gly}$  and  $\text{gly-ala}$ ]", *Eur. J. Mass Spectrom.*, **2001**, *7*, 69 - 78. (O'Hair 70% principal author and joint research supervisor; Styles: PhD student; McFadyen: School of Chemistry collaborator)
- (A45) Kohtani, M.; Jarrold, M.F.; Wee, S.; O'Hair, R. A. J.; "Metal Ion Interactions with Polyalanine Peptides.", *J. Phys. Chem. B*, **2004**, *108*, 6093–6097. (O'Hair 30% joint principal author and joint research supervisor; Kohtani: Indiana University collaborator; Jarrold: joint principal author and Indiana University collaborator; Wee: PhD student)
- (A46) Reid, G.E.; O'Hair, R. A. J.; Styles, M.L.; McFadyen, W.D.; Simpson, R.J., "Gas Phase Ion-molecule Reactions in a Modified Ion Trap: H/D Exchange of Non-covalent Complexes and Coordinatively Unsaturated Platinum Complexes.", *Rapid Commun. Mass Spectrom.*, **1998**, *12*, 1701-1708. "Gas Phase Ion Chemistry of Biomolecules. Part 15" (O'Hair 80% principal author and joint research supervisor; Reid and Styles: PhD students; Simpson: Ludwig Institute for Cancer Research collaborator; McFadyen: School of Chemistry collaborator)
- (A47) O'Hair, R. A. J.; Vrkic, A. K. "Molecular Recognition in the Gas Phase Ligand Switching Reactions of the Proton Bound Dimer of Sarcosine and Glycylglycine.", *Org. Bio. Chem.*, **2003**, *1*, 745 - 750. "Gas Phase Ion Chemistry of Biomolecules. Part 35" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student)



- (A48) Gronert, S.; O'Hair, R. A. J.; Fagan, A.E., "Ion/Molecule Reactions of the Protonated Serine Octamer.", *Chem. Comm*, **2004**, 1944-1945. "Gas Phase Ion Chemistry of Biomolecules. Part 42" (O'Hair 50% joint principal author; Gronert: joint principal author and San Francisco State University Collaborator; Fagan: San Francisco State University Collaborator)
- (A49) Gronert, S.; O'Hair, R. A. J "Gas Phase Reactions of Trimethyl Borate with Phosphates and their Non-Covalent Complexes.", *J. Am. Soc. Mass Spectrom.*, **2002**, *13*, 1088-1098. (O'Hair 40% joint principal author; Gronert: joint principal author and San Francisco State University Collaborator)
- (A50) Vrkic, A. K.; O'Hair, R. A. J. " Gas Phase Reactions of Trimethylborate with the [M-H]<sup>+</sup> ions of Nucleotides and Their Non-covalent Homo and Heterodimer Complexes.", *Aust. J. Chem.*, (Bowie Honour Issue), *Aust. J. Chem.*, **2003**, *56*, 389-399. "Gas Phase Ion Chemistry of Biomolecules. Part 34" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student)
- (A51) Vrkic, A. K.; O'Hair, R. A. J.; Lebrilla C. B. "Unusual Covalent Bond Breaking Reactions of  $\beta$ -Cyclodextrin Inclusion Complexes of Nucleobases and Related Guest Molecules.", *Eur. J. Mass Spectrom.*, **2003**, *9*, 563-577. "Gas Phase Ion Chemistry of Biomolecules. Part 36" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student; Lebrilla University of California (Davis) collaborator)
- (A52) Vrkic, A. K.; O'Hair, R. A. J. "Using Non-Covalent Complexes to Direct the Fragmentation of Glycosidic Bonds in the Gas Phase.", *J. Am. Soc. Mass Spectrom.*, **2004**, *15*, 716-725. "Gas Phase Ion Chemistry of Biomolecules. Part 39" (O'Hair 70% principal author and research supervisor; Vrkic: PhD student))
- (A53) O'Hair, R. A. J.; Sheil, M. M.; Truscott, R. J. W., "Direct Approach to Identification, at the Molecular Level, of Modified Proteins in Human Nuclear Cataractous Lenses:  $\beta$  Crystallin is a Component of the Urea-Insoluble Protein Fraction", *Ophthalmic Res.*, **1992**, *24*, 303-307. (O'Hair, 50% Postdoctoral researcher; Sheil: ANU collaborator; Truscott: principal author and research supervisor)
- (A54) Taverner, T.; O'Hair, R. A. J.; Simpson, R. J. "Characterising Protein-Protein Interactions by Stable Isotope Labelling, Cross-linking and Mass Spectrometry: Application to an Interleukin-6 Dimer", *J. Biol. Chem.* **2002**, *277*, 46487-46492. (O'Hair 20% joint research supervisor; Taverner: honours student; Simpson: principal author and joint research supervisor)
- (A55) Capon, R. J.; Skene, C.; Stewart, M.; Ford, J.; O'Hair, R.A.J.; Williams, L.; Lacey, E.; Gill, J.H.; Heiland, K.; Friedel, T. "Aspergillins A-E: five novel cyclic hexadepsipeptides from the marine-derived fungus *Aspergillus carneus*.", *Org. Bio.*

*Chem.*, **2003**, *1*, 1856 - 1862. (O'Hair 10%; Capon: principal author and School of Chemistry collaborator; Skene, Stewart, Ford, Williams, Lacey, Gill, Heiland, Friedel: School of Chemistry collaborators)

### **Publications (B): Inorganic and Organometallic Gas Phase Ion Chemistry**

- (B1) Damrauer, R.; Krempp, M.; O'Hair, R. A. J., "Gas-Phase Chemistry of  $\text{HSiS}^-$  and  $\text{HSiNH}^-$  : Ions Related to Silathioformaldehyde and the Silaazomethine of Formaldehyde", *J. Am. Chem. Soc.*, **1993**, *115*, 1998-2005. (O'Hair 30% Postdoctoral researcher; Krempp: Postdoctoral researcher; Damrauer: principal author and research supervisor)
- (B2) Shimizu, H.; Gordon, M. S.; Damrauer, R.; O'Hair, R. A. J., " Potential Energy Surface of the Reaction of the Silaformyl Anion and  $\text{CO}_2$ ", *Organometallics*, **1995**, *14*, 2664-2671. (O'Hair, 10% Postdoctoral researcher; Shimizu: Iowa State University collaborator; Gordon and Damrauer principal authors and research supervisors)
- (B3) O'Hair, R. A. J.; Krempp, M.; Damrauer, R.; DePuy, C. H., "Gas-Phase Ion Chemistry of  $\text{HP}_2^-$ ,  $\text{FP}_2^-$  and  $\text{HP}_2^+$  ", *Inorg. Chem.*, **1992**, *31*, 2092-2096. (O'Hair, 60% Postdoctoral researcher; Krempp: Postdoctoral researcher; Damrauer and DePuy principal authors and research supervisors)
- (B4) O'Hair, R. A. J.; DePuy, C. H.; Bierbaum, V. M., "Gas-Phase Chemistry and Thermochemistry of the Hydroxysulfide Anion,  $\text{HOS}^-$ ", *J. Phys. Chem.*, **1993**, *97*, 7955-7961. (O'Hair, 60% Postdoctoral researcher; DePuy: University of Colorado collaborator; Bierbaum: principal author and research supervisor)
- (B5) Downard, K. M.; Bowie, J. H.; O'Hair, R. A. J.; Krempp, M.; DePuy, C. H., "Gas Phase Reactions of the Methylsulfinyl and Methyldisulfide Anions", *Int. J. Mass Spectrom. Ion Proc.*, **1992**, *120*, 217-229. (O'Hair, 25% Postdoctoral researcher; Downard: University of Adelaide collaborator; Krempp: University of Colorado collaborator; Bowie and DePuy principal authors and research supervisors)
- (B6) Smith, J. D.; O'Hair, R. A. J., "Reactions of Phosphorus Trifluoride with Anionic Nucleophiles in the Gas Phase.", *Eur. Mass Spectrom.*, **1996**, *2*, 225-231. (O'Hair 80% principal author and research supervisor; Smith: MS student)
- (B7) Smith, J. D.; O'Hair, R. A. J., "Gas Phase Reactions of Dialkoxydisulfides, ROSSOR (R =  $\text{CH}_3$  and  $\text{CH}_3\text{CH}_2$ ), with Anionic Nucleophiles", *Phos. Sulf. Silicon Rel. Elements*, **1997**, *126*, 257-272. (O'Hair 80% principal author and research supervisor; Smith: MS student)

- (B8) Smith, J. D.; O'Hair, R. A. J.; Williams, T. D., "Gas Phase Chemistry of Sulfonate Anions: Basicities and Fragmentation Reactions.", *Phos. Sulf. Silicon Rel. Elements*, **1996**, *119*, 49-59. (O'Hair 80% principal author and research supervisor; Smith: MS student; Williams: University of Kansas collaborator)
- (B9) Styles, M. L.; O'Hair, R. A. J.; McFadyen, W.D.; Tannous, L.; Holmes, R.J.; Gable, R.W., "Formation and Gas Phase Fragmentation Reactions of Ligand Substitution Products of Platinum(II) Complexes via Electrospray Ionization Tandem Mass Spectrometry." *J. Chem. Soc., Dalton Trans.*, **2000**, 93-99. (O'Hair 50% principal author and joint research supervisor; Styles and Holmes: PhD students; Tannous: Honours student; McFadyen and Gable: School of Chemistry collaborators)
- (B10) Wee, S.; Grannas, M.J.; McFadyen, W.D.; O'Hair, R. A. J "Gas-Phase and Condensed-Phase Studies on the Reactivity of the Azido(2,2':6',2''-terpyridine)-platinum(II) Cation.", *Aust. J. Chem.*, **2001**, *54*, 245-252. (O'Hair 50% joint principal author and joint research supervisor; Wee: honours student; McFadyen: joint principal author and joint research supervisor; Grannas: School of Chemistry collaborator)
- (B11) Wee, S.; White, J.M.; McFadyen, W.D., O'Hair, R.A.J "Gas-phase studies on the reactivity of the azido(diethylenetriamine)platinum(II) cation and derived species." *Aust. J. Chem.*, **2003**, *56*, 1201-1207. (O'Hair 50% joint principal author and joint research supervisor; Wee: honours student; McFadyen: joint principal author and joint research supervisor; White: School of Chemistry collaborator)
- (B12) Wee, S.; O'Hair, R. A. J.; McFadyen, W.D., "Gas Phase Ligand Loss and Ligand Substitution Reactions of Platinum(II) Complexes of Tridentate Nitrogen Donor Ligands.", *Rapid Commun. Mass Spectrom.*, **2004**, *18*, 1221-1226. (O'Hair 50% joint principal author and joint research supervisor; Wee: honours student; McFadyen: joint principal author and joint research supervisor)
- (B13) Holmes, R.J.; O'Hair, R. A. J.; McFadyen W.D., "ESI/MS/MS Studies of Competitive Pyridine Loss From Platinum(II) Ethylenediamine Complexes by the Kinetic Method" *Rapid Commun. Mass Spectrom.*, **2000**, *14*, 2385-2392. (O'Hair 70% principal author; Holmes: PhD student; McFadyen: School of Chemistry collaborator and research supervisor)
- (B14) Liyanage, R.; Styles, M. L.; O'Hair, R. A. J.; Armentrout, P. B. "Sequential Bond Energies of  $\text{Pt}(\text{NH}_3)_x^+$  ( $x = 1 - 4$ ) Determined by Collision-induced Dissociation and Theory", *Int. J. Mass Spectrom.*, (invited contribution to Professor Dunbar Honour Issue), **2003**, *227*, 47 - 62. (O'Hair 10%; Liyanage: University of Utah collaborator; Styles: PhD student; Armentrout: principal author and University of Utah collaborator)

- (B15) Liyanage, R.; Styles, M. L.; O'Hair, R. A. J.; Armentrout, P. B. "Guided Ion Beam and Ab initio Studies of Platinum Chloride Cations", *J. Phys. Chem. A*, **2003**, *107*, 10303-10310. (O'Hair 10%; Liyanage: University of Utah collaborator; Styles: PhD student; Armentrout: principal author and University of Utah collaborator)
- (B16) Waters, T.; O'Hair, R. A. J.; Wedd, A. G. " Probing the Catalytic Oxidation of Alcohols via an Anionic Dimolybdate Centre Using Multistage Mass Spectrometry." *Chem. Comm.*, **2000**, 225-226. (O'Hair 60% principal author and joint research supervisor; Waters: PhD student; Wedd: principal author, joint research supervisor and School of Chemistry collaborator)
- (B17) Waters, T.; O'Hair, R. A. J.; Wedd, A. G. "Catalytic Gas Phase Oxidation of Methanol to Formaldehyde.", *J. Am. Chem. Soc.*, **2003**, *125*, 3384-3396. (O'Hair 60% principal author and joint research supervisor; Waters: PhD student; Wedd: principal author, joint research supervisor and School of Chemistry collaborator)
- (B18) Waters, T.; O'Hair, R. A. J.; Wedd, A. G. " Catalytic Gas Phase Dehydration of Acetic Acid to Ketene. ", *Int. J. Mass Spectrom.*, (invited contribution to Professor Schwarz Honour Issue), **2003**, *228*, 599 - 611. (O'Hair 60% principal author and joint research supervisor; Waters: PhD student; Wedd: joint research supervisor and School of Chemistry collaborator)
- (B19) Feyel, S.; Waters, T.; O'Hair, R. A. J.; Wedd, A.G., "Gas Phase Oxidation of Alkoxo Ligands in Bis(peroxo)  $[MO(O_2)_2(OR)]^-$  and Trisoxo  $[MO_3(OR)]^-$  Anions (M = Cr, Mo, W).", *Dalton Trans.*, **2004**, 4010 - 4016. (O'Hair 40% principal author and joint research supervisor; Feyel: visiting graduate student; Waters: PhD student; Wedd: principal author, joint research supervisor and School of Chemistry collaborator)
- (B20) Waters, T.; Wang, X.-B.; Yang, X.; Zhang, L.; O'Hair, R. A. J.; Wang, L.-S.; Wedd, A. G. " Photoelectron Spectroscopy of the Doubly-Charged Anions  $[M^{IV}O(mnt)_2]^{2-}$  (M = Mo, W;  $mnt = S_2C_2(CN)_2^{2-}$ ): Access to the Ground and Excited States of the  $[M^V O(mnt)_2]^-$  Anion.", *J. Am. Chem. Soc.*, **2004**, *126*, 5119-5129. (O'Hair 10%; Waters: PhD student; Wang, Yang, Zhang: PNNL collaborators.; Wang: joint principal author and PNNL collaborator; Wedd: joint principal author, joint research supervisor and School of Chemistry collaborator)
- (B21) Yang, X.; Waters, T.; Wang, X.-B.; O'Hair, R. A. J.; Wedd, A.G.; Dixon, D.A.; Li, J.; Wang, L.S.; "Photoelectron Spectroscopy of Free Polyoxoanions  $Mo_6O_{19}^{2-}$  and  $W_6O_{19}^{2-}$  in the Gas Phase.", *J. Phys. Chem. A*, **2004**, *108*, 10089-10093. (O'Hair 10%; Waters: PhD student; Yang, Wang, Dixon, Li: PNNL collaborators; Wedd: School of Chemistry collaborator; Wang: principal author and PNNL collaborator)

- (B22) O'Hair, R. A. J "Dimethylargenate is a stable species in the gas phase." *Chem. Comm.*, **2002**, 20 - 21. (O'Hair 100%)
- (B23) James, P. F.; O'Hair, R. A. J., "Dimethyl cuprate undergoes C-C bond coupling with methyl iodide in the gas phase but dimethyl argenate does not.", *Org. Lett.*, **2004**, *6*, 2761-2764. (O'Hair 70% principal author and research supervisor; James: undergraduate student)
- (B24) O'Hair, R. A. J.; Vrkic, A. K.; James, P. F., "Gas Phase Synthesis and Reactivity of the Organomagnesates [CH<sub>3</sub>MgL<sub>2</sub>] (L = Cl and = O<sub>2</sub>CCH<sub>3</sub>): From Ligand Effects to Catalysis.", *J. Am. Chem. Soc.*, **2004**, *126*, 12173-12183. (O'Hair 70% principal author and research supervisor; Vrkic: PhD student; James: undergraduate student)
- (B25) Khairallah, G.N.; O'Hair, R. A. J., " Gas Phase Synthesis of Ag<sub>4</sub>H<sup>+</sup> and its Mediation of C-C Bond Coupling of Allylbromide.", *Angew. Chem. Int. Ed.*, in press. (O'Hair 70% principal author and research supervisor; Khairallah: postdoctoral researcher)

### Publications (C): Organic Gas Phase Ion Chemistry

- (C1) Damrauer, R.; Krempp, M.; O'Hair, R. A. J.; Simon, R., "The Gas Phase Acidities of Hindered Amines and Some Reaction Chemistry of their Corresponding Amide Ions", *Int. J. Mass Spectrom. Ion Proc.*, **1992**, *117*, 199-211. (O'Hair, 25% Postdoctoral researcher; Krempp and Simon: University of Colorado collaborators; Damrauer principal author and research supervisor)
- (C2) O'Hair, R. A. J.; Davico, G. E.; Hacaloglu, J.; Dang, T. T.; DePuy, C. H.; Bierbaum, V. M., "Measurement of Solvent and Secondary Kinetic Isotope Effects for the Gas-Phase S<sub>N</sub>2 Reactions of Fluoride with Methyl Halides", *J. Am. Chem. Soc.*, **1994**, *116*, 3609-3610. (O'Hair, 40% Postdoctoral researcher; Davico, Hacaloglu, Dang, DePuy: University of Colorado collaborators; Bierbaum: principal author and research supervisor)
- (C3) O'Hair, R. A. J.; Androustopoulos, N. K., " Can Transacylation Reactions Occur via S<sub>N</sub>2 Pathways in the Gas Phase? Insights via Ion-Molecule Reactions of N-Acylpyridinium ions and *Ab Initio* Calculations.", *Org. Lett.*, **2000**, *2*, 2567-2570. (O'Hair 90% principal author and research supervisor; Androustopoulos: honours student)
- (C4) Vrkic, A. K.; O'Hair, R. A. J.; "Gas Phase Ion Chemistry of Para Substituted Benzene Diazonium Ions, Their Salt Clusters and Their Related Phenyl Cations.", *Int. J. Mass Spectrom.*, **2002**, *218*, 131-160. (O'Hair 70% principal author and research supervisor; Vrkic: PhD student)

- (C5) Sheldon, J. C.; O'Hair, R. A. J.; Downard, K. M.; Gronert, S.; Krempp, M.; DePuy, C.H.; Bowie, J. H., "A Potential Surface Map of the H<sup>-</sup>/N<sub>2</sub>O System. The Gas Phase Ion Chemistry of HN<sub>2</sub>O<sup>-</sup>", *Aust. J. Chem.*, **1995**, *48*, 155-165. (O'Hair, 35% Postdoctoral researcher; Sheldon and Downard: University of Adelaide collaborators; Gronert and Krempp: University of Colorado collaborators; Bowie and DePuy principal authors and research supervisors)
- (C6) O'Hair, R. A. J.; Gronert, S.; DePuy, C. H., "New Insights into the Gas-Phase Anion Chemistry of Nitrous Oxide.", *Eur. Mass Spectrom.*, **1995**, *1*, 429-436. (O'Hair, 50% Postdoctoral researcher and principal author; Gronert and DePuy: University of Colorado collaborators)
- (C7) Sheldon, J. C.; Bowie, J. H.; Dua, S.; Smith, J. D.; O'Hair, R. A. J., "The Gas Phase Cannizzaro Disproportionation Reactions of Benzaldehyde and Pivaldehyde.", *J. Org. Chem.*, **1997**, *62*, 3931-3937. (O'Hair 15%; Sheldon and Dua: University of Adelaide collaborators; Bowie principal author; Smith: MS student)
- (C8) Waters, T.; Blanksby, S.J.; Zhang, L.; O'Hair, R. A. J.; "Formation of the Heterocumulene Anion SCCCN<sup>-</sup> by a Cyano Migration from the Radical Anion of 1,2-dicyanoethylenedithiolate.", *Org. Bio. Chem.*, **2004**, *2*, 190-194. (O'Hair 50% joint principal author; Waters: PhD student; Blanksby: joint principal author and University of Wollongong collaborator; Zhang: School of Chemistry collaborator)

### International Patent

- (D1) **International Application No. PCT/US03/36739. Filed with US Patent & Trademark Office:** November 18, 2003. **Title of Invention:** Method for analysing amino acids, peptides and proteins; **Inventors:** Reid, G. E.; Simpson, R. J.; O'Hair, R. A. J. (all inventors: 33%) **Awarded:** 2004 (listed in Chemical Abstracts as CAN 140: 420 396).

### Invited Reviews

- (E1) O'Hair, R. A. J.; "Anion-Molecule Reactions of Organophosphorus and Organosulfur Species: Some Mechanistic Aspects", *Mass Spectrom. Rev.*, **1991**, *10*, 133-173. (O'Hair 100%)
- (E2) O'Hair, R. A. J., "Designer Reactions: Biomolecules in the Gas Phase.", *Chemistry in Australia*, **1998**, September Issue, 50-53. (O'Hair 100%)
- (E3) O'Hair, R. A. J. "The Role of Nucleophile-Electrophile Interactions in the Unimolecular and Bimolecular Gas Phase Ion Chemistry of Peptides and Related Systems", *J. Mass Spectrom.*, **2000**, *35*, 1377-1381. (O'Hair 100%)

- (E4) O'Hair, R. A. J., "Organic Gas Phase Ion Chemistry", *Annu. Rep. Prog. Chem., Sect. B*, Chapter 8, **2001**, 393-455. (O'Hair 100%)
- (E5) Waters, T.; O'Hair, R. A. J., "Organic Gas Phase Ion Chemistry", *Annu. Rep. Prog. Chem., Sect. B*, Chapter 9, **2002**, 433-501. (Waters 50%, O'Hair 50%)
- (E6) O'Hair, R. A. J.; Khairallah, G.N., "Gas Phase Ion Chemistry of Transition Metal Clusters: Production, Reactivity and Catalysis.", *J. Cluster Sc.*, **2004**, 3, 331-363. (O'Hair 50%, Khairallah 50%)

### Invited Book Chapters

- (F1) O'Hair, R. A. J., "Gas-Phase Positive and Negative Ion Chemistry of Organophosphorus Compounds via Mass Spectrometric Techniques", in "The Chemistry of Organophosphorus Compounds - Volume 4" (Hartley, F.R.; Ed.; ISBN: 0-471-95706-2), Wiley, New York, Chapter 8, **1996**, 731-765. (O'Hair 100%)
- (F2) O'Hair, R. A. J., "Ion Chemistry and Fragmentation", in "Mass Spectrometry in Drug Discovery" (Rossi, D.T.; Sinz, M.W.; Eds.; ISBN: 0-8247-0607-2), Marcel Dekker, New York, Chapter 4, **2002**, 85 - 124. (O'Hair 100%)
- (F3) Rossi, D.T.; O'Hair, R. A. J., "Future Prospects", in "Mass Spectrometry in Drug Discovery" (Rossi, D.T.; Sinz, M.W.; Eds.; ISBN: 0-8247-0607-2), Marcel Dekker, New York, Chapter 13, **2002**, 399 - 413. (Rossi 70%, O'Hair 30%)
- (F4) O'Hair, R. A. J., "Fragmentation mechanisms of protonated peptides in the gas phase." In: Simpson, R.J. "Proteins and Proteomics: A Laboratory Manual" (ISBN: 0-8247-0607-2), Cold Spring Harbor Laboratory Press, New York, Chapter 8, **2003**, 577 - 584. (O'Hair 100%)

### Invited Encyclopedia Contributions

- (G1) O'Hair, R. A. J., Contribution to "The Encyclopedia of Mass Spectrometry" (Gross, M.L. and Caprioli, R. Eds. in Chief), Volume 1: Theory and Ion Chemistry (Armentrout, P. Ed. ISBN: 0-08-043802-4), Elsevier, Amsterdam, Chapter 9: Organic Ion Chemistry (Positive), Topic: "S<sub>N</sub>2 and related reactions", **2003**, 604-619. (O'Hair 100%)
- (G2) Damrauer, R.; O'Hair, R. A. J., Contribution to "The Encyclopedia of Mass Spectrometry" (Gross, M.L. and Caprioli, R. Eds. in Chief), Volume 1: Theory and Ion Chemistry (Armentrout, P. Ed. ISBN: 0-08-043802-4), Elsevier, Amsterdam, Chapter 10: Organic Ion Chemistry (Negative), Topic: "Organo-aluminum, -silicon, -phosphorus, and -sulfur Chemistry", **2003**, 674-686. (Damrauer 50%, O'Hair 50%)
- (G3) Waters, T.; O'Hair, R. A. J., Contribution to "Encyclopedia of Mass Spectrometry", Volume 7. Fundamentals of and Applications to Organic (and Organometallic)

Compounds (Nibbering, N.M.M. Ed.), General Subject Area G. Metal Ion Complexes: Formation and Reactivity, Topic: "G14. Organometallic catalysis in the gas phase", **2004**, in press. (Waters 50%, O'Hair 50%)

#### **Other Invited Scientific Publications**

- (H1) **Book Review:** O'Hair, R. A. J.; Derrick, P.J, *Eur. J. Mass Spectrom.*, **2002**, 8, 333-335, review of "Interpreting Protein Mass Spectra" by A Peter Snyder, Published by Oxford University Press Inc, New York, USA, Copyright 2000 ISBN 0-841-23571-6.
- (H2) **News and Views Announcement:** Green, A.; O'Hair, R. A. J.; "Professor John Bowie Festschrift." *Chemistry in Australia*, **2003**, 70(4, May Issue), 36.
- (H3) **Editorial and Biographical Sketch:** O'Hair, R. A. J.; "John Hamilton Bowie: An Appreciation" *Aust. J. Chem.*, **2003**, 56, 343-348.
- (H4) **Editorial and Historical Sketch:** O'Hair, R. A. J.; "The Australian and New Zealand Society for Mass Spectrometry Conference – A Tradition of Over Thirty Years." *Eur. J. Mass Spectrom.*, **2003**, 9, 525-529.



## Publications (A): Gas Phase Ion-Chemistry and Mass Spectrometry of Biomolecules

NOTE:

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