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BARBARA CHIAVARINO
Curriculum Vitae

Place Roma
Date July, 4Th,2018

Part I – General Information

Full Name	Barbara Chiavarino
Spoken Languages	Italian, French, English

Part II – Education

Type	Year	Institution	Notes (Degree, Experience, …)
University graduation	1992	Sapienza Università di Roma	Laurea (Master Degree) in Pharmaceutical Chemistry and Technology, 110/110
Post-graduates studies	1996	Sapienza Università di Roma	PhD in Pharmaceutical Sciences (Dottorato di ricerca in Scienze Farmaceutiche, VIII Ciclo)
Licensure	1992	Sapienza Università di Roma	Qualification as Pharmacist

Part III – Appointments

IIIA – Academic Appointments

Start	End	Institution	Position
1/10/1998	to the present	Sapienza Università di Roma	Research associate (Ricercatore Universitario)
Call 2013 (1/12/2014)	01/12/2020	Ministero dell'Istruzione dell'Università e della Ricerca (MIUR)	National Scientific Qualification (ASN) as associate professor (Professore di II fascia, Settore Concorsuale 03/B1 – Fondamenti delle Scienze Chimiche e Sistemi Inorganici, SSD CHIM/03)

Call 2012 (17/02/2014)	17/02/2020	Ministero dell'Istruzione dell'Università e della Ricerca (MIUR)	National Scientific Qualification (ASN) as associate professor (Professore di II fascia, Settore Concorsuale 03/B2 – Fondamenti Chimici delle Tecnologie, SSD CHIM/03)

IIIB – Other Academic Appointments

Start	End	Institution	Position
2017	to the present	Sapienza Università di Roma	Member of the board of the Faculty of Pharmacy and Medicine (membro della giunta della Facoltà di Farmacia e Medicina, in qualità di rappresentante dei ricercatori del dipartimento di Chimica e Tecnologie del Farmaco)
2008	2018	Sapienza Università di Roma	Member of the board of the Department of Pharmaceutical Chemistry and Technology (membro della giunta del consiglio di Dipartimento di Chimica e Tecnologie del Farmaco, in qualità di rappresentante dei ricercatori)
2005	2008	Sapienza Università di Roma	Member of the board of the Department of Studies in Chemistry and Technologies of Biologically Active Substances(membro della giunta del consiglio di Dipartimento di Studi di Chimica e Tecnologie delle Sostanze Biologicamente Attive, in qualità di rappresentante dei ricercatori)
2017	to the present	Sapienza Università di Roma	Member of the training committee for the degree course in Applied Pharmaceutical Sciences (commissione tirocino per il corso di Scienze Farmaceutiche Applicate, SFA)
2010	to the present	Sapienza Università di Roma	Member of the Department committee for the maintenance and spaces (commissione manutenzione edilizia e spazi)
2013	-	Sapienza Università di Roma	Member of evaluation committee for post doc fellowship
2009	2012	Sapienza Università di Roma	Member of the teaching and quality committee for the degree course in Scientific Information on Drugs (commissione didattica e qualità)
	to the present	Sapienza Università di Roma	Supervisor for master degree theses in "Chimica e Tecnologia Farmaceutiche" (CTF) and in "Farmacia", Supervisor for degree theses in "Informazione Scientifica sul Farmaco" (ISF)and in "Scienze Farmaceutiche Applicate" (SFA)
	to the present	Sapienza Università di Roma	Supervisor for training for students of the degree in ISF and in SFA

IIIC – Other Appointments

Start	End	Institution	Position
1997	-	Universität Bielefeld- Germany	Short term visit at the Prof. Hans-Friedrich Grützmacher laboratories – 2 months
01/04/1996	31/03/1997	Italian National Research Council (CNR)	Winner of a Grant in Chemical Sciences
1994	-	University of Nantes and the Eurofins Industry- Nantes- France	Winner of a COMETT grant (Programma comunitario di istruzione e formazione nel settore della tecnologia per estendere e incoraggiare la cooperazione tra università e industria nel campo della formazione legata alle nuove tecnologie) at the Prof. G. Matin laboratories and the Eurofins Industry - 6 months

Part IV – Teaching experience

Year	Institution	Lecture/Course
2017-today	Sapienza Università di Roma	"General and Inorganic Chemistry", canale A-L, degree course SFA, 9 CFU
2017	Université of Paris-Sud	"Méthodes avancées de spectroscopie" for the M2 degree in Physical Chemistry at the Facultè des Sciences d'Orsay as invited professor
2017-today	Sapienza Università di Roma	"General and Inorganic Chemistry", canale A-L, lezioni a piccoli gruppi, master degree course CTF, 3 CFU
2010 -2017	Sapienza Università di Roma	"General and Inorganic Chemistry", canale unico, degree course SFA, 9 CFU
2001-2009	Sapienza Università di Roma	"General and Inorganic Chemistry", canale unico, degree course ISF, 10 CFU
1999-2002	Sapienza Università di Roma	"Chemistry of coordination compounds", master degree course CTF

Part V - Society memberberships, Awards and Honors

Year	Title
2009 -	Member of the Italian Chemical Society (SCI)

2016	Scuderi, D., Bodo, E., Chiavarino, B., Fornarini, S., Crestoni, M.E. "Amino Acid Oxidation: A Combined Study of Cysteine Oxo Forms by IRMPD Spectroscopy and Simulations" *Chemistry - A European Journal* (2016), 22 (48), pp. 17239-17250 – **2016 Back Cover of the issue**
2016	Corinti, D., Crestoni M. E., Fornarini, S., Chiavarino, B. "Distinction between cyanidine 3-O-glucoside and cyanidine 3-O-galactoside by mass spectrometry combined with IRMPD spectroscopy" Convegno Massa 2016, Istituto Superiore di Sanità, Roma, 6-8 settembre, 2016. – **Best Poster award**
2015	Corinti, D., Coletti, C., Re, N., Chiavarino, B., Crestoni, M. E., Fornarini, S. "*Cis*platin reactions with model biological ligands monitored by IR multiphoton dissociation spectroscopy" - XLIII Congresso Nazionale della Divisione di Chimica Inorganica della Società Chimica Italiana – Camerino, 9-12 settembre 2015. – **Best Poster award**
2007	Chiavarino, B., Crestoni, M.E., Fornarini, S., Lanucara, F., Lemaire, J., Maître, P. "Meisenheimer complexes positively characterized as stable intermediates in the gas phase" *Angewandte Chemie - International Edition,* (2007) 46 (12), pp. 1995-1998.- **Very Important paper mention**
1999	Chiavarino, B., Crestoni, M.E., Di Marzio, A., Fornarini, S., Rosi, M. "Electrophilic substitution of gaseous borazine" Journal of the American Chemical Society, (1999), 121 (11), pp. 2619-2620. - **special mention in Chemical & Engineering News (*C&EN*) MARCH 22,1999**

Part VI – Other Activities

Year	Title
2004 -	Oral or poster presentations at national and international conferences: 12
1998 -	Collaboration with international research groups: • Prof. Philippe Maitre, CNRS and Université Paris-Sud, France • Dr Jean-Yves Salpin, Université d'Evry Val d'Essonne, CEA, CNRS, Université Paris-Saclay, F-91025, Evry, France • Dr Debora Scuderi, Université Paris Sud Orsay, CNRS, Université Paris-Saclay, F-91405 Orsay, France • Prof. Otto Dopfer Technische Universität Berlin, Germany • Prof. Carme Rovira, Universitat de Barcelona, Spain • Dr. Gilles Frison CNRS - Ecole Polytechnique Paris-Saclay, France • Prof. Hans-Ullrich Siehl , Universität Ulm, Germany • Dr Riccardo Spezia. Sorbonne Universités, Univ Paris 6, France • Prof. Dietmar Kuck, Universität Bielefeld, Germany • Dr. Rajeev K. Sinha, Manipal University, India
2007-	Reviewer for several scientific international journals including : J. Phys Chem A, Chem Phys Lett., Phys.Chem.Chem.Pys., Analytical Letters, International Journal of Mass Spectrometry, ChemPhysChem.
2004-2008	Member of three selection boards for comparative evaluations for a position as researcher associate SSD CHIM/03 – Chimica Generale ed Inorganica • Università di Firenze con nomina nella gazzetta ufficiale (GU n.92 del 19-11-2004). Sede

	della valutazione comparativa: Dipartimento di Chimica, via della Lastruccia, 3 - 50019 Sesto F.no (FI). • Università degli studi di Palermo con nomina nella gazzetta ufficiale (GU n.93 del 25-11-2005). Sede della valutazione comparativa: Dipartimento di Chimica Inorganica e Analitica, Viale delle Scienze, Parco d'Orleans II Palermo • Università degli studi di Catania con nomina nella gazzetta ufficiale (GU n 59 del 29-07-2008). Sede della valutazione comparativa: Dipartimento di Scienze del Farmaco Città Universitaria - Viale Andrea Doria, 6 - 95125 - Catania

Part VII - Funding Information [grants as PI-principal investigator or I-investigator]

Year	Title	Program
2017	Interazioni del *cis*platino con 2'-deossiadenosina-5'-monofosfato e dinucleotidi: un'indagine tramite spettroscopia IR, spettrometria di massa e calcoli teorici **as Principal Investigator**	Sapienza Università di Roma (Ateneo) Grant: RP11715C6456718F
2017	Fondo per il Finanziamento della Attività Base di Ricerca - FFABR	MIUR
2017	IRMPD Spectroscopy study on the role of (non)covalent bonded halogens on simple biomolecules **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center (Centre Laser Infrarouge d'Orsay), France. – Project IC17-002
2016	IRMPD spectroscopy to characterize biologically active substances: micronutrients and tumor growth inhibitors **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC16-007
2015	Interaction of carboplatin and oxaliplatin with nucleic acids: an approach by IRMPD spectroscopy **as Principal Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC15-014
2015	IRMPD spectroscopy to characterize biologically active substances: food components and additives **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC15-007
2014	Probing *cis*platin drug carriers by IRMPD spectroscopy **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC14-011
2013	Structural and electronic features of naked Iron(II/III) nitrosyl complexes: Searching evidence for spin crossover phenomena **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC13-014
2012	The interaction of *cis*platin with nucleic acids: an approach by IRMPD spectroscopy. II	European Union funding for access to the IR free electron laser

	as Principal Investigator	beamline of the CLIO center, France. - Project IC 019-12
2011	The interaction of *cis*platin with nucleic acids: an approach by IRMPD spectroscopy. **as Principal Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 007-11
2011	Fari 2011 **as Principal Investigator**	Sapienza Università di Roma (Ateneo) Grant: C26/11CHR5
2011	Applications of IRMPD spectroscopy to identify post-translational modifications of amino acids and peptides: nitro, nitroso and sulfonyl features **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 009-11
2010	Spectroscopic properties of nitroso amino acids as isolated ionic species **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 008-10
2010	Reattività e struttura di complessi ionici bioinorganici **as Investigator**	Sapienza Università di Roma (Ateneo) Grant: C26A10577L
2009	Reattività e struttura di ioni silile in fase gassosa **as Principal Investigator**	Sapienza University of Roma (Facoltà): Grant n.277/09
2009	Elusive intermediates in elementary processes of naked biomolecules **as Investigator**	PRIN Grant: 2009W2W4YF_00
2009	Spectroscopic study of structural motifs of bare anion-arene interaction **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 021-09
2008	Heme group activity probed by IRMPD-2 **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 023-08
2007	Heme group activity probed by IRMPD-1 **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 016-07
2007	Reattività e struttura di intermedi ionici di interesse bioinorganico e fondamentale **as Investigator**	Sapienza Università di Roma (Ateneo) Grant: C26A07NNXN
2006	Spectroscopie infrarouge couplée à la spectrométrie de masse: caractérisation structurale d'intermédiaires réactionnels **as Investigator**	French Italian exchange project PICS 2006 (Project International de Cooperation Scientifique)
2006	Struttura, dinamica ed energetica di complessi ionici e sistemi chirali in fase gassosa **as Investigator**	PRIN Grant: 2006 2006038520_005

2005	IRMPD as a probe of heme cation binding to NO and simple biological ligands **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 007-05
2005	Specie cariche isolate: modelli di interesse fondamentale e di attività biomimetica **as Investigator**	Sapienza Università di Roma (Ateneo) Grant: C26A051325
2004	Protonated inorganic acids assayed by IR multiphoton dissociation **as Investigator**	European Union funding for access to the IR free electron laser beamline of the CLIO center, France. - Project IC 006-04
2000	Reattività di Cationi Radicali in Fase gassosa **as Principal Investigator**	MURST "Progetto Giovani Ricercatori" Grant G113725

Part VIII – Research Activities

Keywords

- Tandem mass spectrometry
- Infrared spectroscopy of gaseous ions
- Ion-molecule reactions
- structural characterization
- Kinetics, energetics, and chemical reaction mechanisms of ionic intermediates;
- Intermolecular interactions (ion-ligand interactions, hydrogen bonds, ion-pi interactions, molecular recognition of biological systems
- Untargeted analysis of foodstuff

Brief Description

The main issue in my research activity regards the study of the structure and reactivity of ionic species in the gas phase. The advantage of carrying out an investigation in the gas phase is related to the dilute environment lacking solvation and ion pairing effects, typical of the condensed phase. Thereby, it becomes possible to highlight the intrinsic reactivity of ions, thus offering a valid reference for theoretical calculations and an insight into the influence of the solvent in solution. This approach has relevance for the understanding of complex processes occurring in interstellar space, in flames ending, up to the hydrophobic environment of some enzymatic sites. The studies that I am presenting here have been carried out exploiting, and often combining, three complementary methodologies, namely the gamma radiolytic technique, the Fourier transform ion-cyclotron resonance mass spectrometry (FT-ICR MS) and the InfraRed Multiple Photon Dissociation (IRMPD) spectroscopy.

The radiolytic technique allows to generate ions through the effect of ionizing gamma-radiation on suitable neutral gases hold in glass bulbs at relatively high-pressure regimes (about 1 atm). Under such conditions, the radiolytically formed ions may undergo efficient thermal equilibration by non-reactive collisions with the neutral precursor prior to interact with selected substrates and give rise to the neutral end products. The reactivity of the thermalized ions is measured by standard kinetic procedures, including temperature and

pressure dependence studies and competition experiments. The characterization of the neutral end products is achieved by using analytical techniques such as gas-chromatography coupled to mass spectrometry (GC-MS) and NMR spectroscopy, so providing valuable information about the regio-and stereochemistry of the ionic process under investigation under thermal equilibrium conditions. The radiolytic technique may be applied only to volatile or easily volatilized substrates.

FT-ICR mass spectrometry operates in a very low-pressure regime, in the range of 1-10 × 10^{-8} mbar, where the initial energy content of the reaction partners can be considered constant and the bimolecular reactions take place in a single collision regimen. This tool allows to mass-select a specific ion of interest from a very complex ionic population, identify its molecular formula by high resolution mass measurements and distinguish among isomeric compounds with same integer mass, but different chemical formulas. In addition, the ion trapping ability of FT-ICR MS enables the reactivity behavior towards selected neutrals to be investigated. In this way, isomeric species can be kinetically characterized and distinguished. FT-ICR MS does also allow to determine: i) the rate constants of ion-molecule reactions occurring through multiple parallel or consecutive channels; ii) fundamental thermodynamic parameters, such as enthalpies and Gibbs free reaction energies and the heat of formation of ionic and neutral species, through the attainments of equilibrium constants.

IRMPD spectroscopy is a powerful tool to perform structural characterization of ionic species in the isolated state. The direct spectroscopic assay of bare species has become possible after the coupling of a bright IR laser source with a modified mass spectrometer (FT-ICR or Paul trap). This combination overcomes the difficulty related to the low density of gaseous ions stored inside the ion trap. The studies presented here have taken advantage of two different experimental platforms. For the mid-IR (600-2000 cm^{-1}), the intense and tunable IR radiation of the free electron laser (FEL) beamline at the Centre Laser Infrarouge d'Orsay (CLIO) at Université Paris XI was used. The experiments were carried out in collaboration with Philippe Maître and his team and allowed us to record IR spectra of gaseous ions, in the absence of perturbations due to solvent, matrix or counter-ions. The second, more recent coupling has been achieved at Sapienza Università di Roma and uses a benchtop optical parametric oscillator/amplifier (OPO/A) laser associated with an ion-trap. This apparatus allows to record IR spectra of mass-selected ions in the X-H stretching range (X = C, N, O) (2800 -4000 cm^{-1}). The non-coherent absorption of multiple IR photons may induce fragmentation of the selected ion within the ion trap. IR induced fragmentation is only observed on resonance with an IR active vibrational mode of the selected ion. IRMPD spectra are obtained by plotting the photofragmentation yield as a function of the frequency of the IR radiation in the two spectral ranges. Experimental studies are backed by ab initio theoretical calculations. The comparison between the IRMPD spectra and the IR absorption spectra calculated for the most stable structures may allow the structural assignment of the sampled ions and highlight the preferred conformations in the gas phase. This result is unprecedented and has been exploited to address the characterization of metal cation binding patterns, natural and modified amino acids and peptides, halide complexes, simple (in)organic species of fundamental interest. In most cases, the ionic species are formed in solution and then driven in the gas phase by electrospray ionization.

The description of my research reported here refers to the 12 selected publications (reported as Selected Publication **A1-A12**) and to the publications listed in the attached file (Allegato E) "Publications list" (reported as Publication P1-P82).

My current research is mainly carried out at the Dipartimento di Chimica e Tecnologie del Farmaco in collaboration with several Italian and foreign teams. The IRMPD spectroscopy in the fingerprint range of the IR

spectrum is achieved using IR radiation of free electron lasers at the Laser Infrarouge d'Orsay Center facility (Clio) accessed by presenting annually projects submitted to peer review and funded by the European Union.

Briefly, the subjects of my recent research and the main achievements can be described as follows:

(a) *Reactivity and structural issues regarding a Platinum-based anticancer drug*

Ionic species deriving from the interaction of aqueous *cis*- and *trans*platin complexes with DNA bases, nucleotides, and natural amino acids, responsible for the drug activity and side effects, respectively, have been investigated by applying MS techniques coupled with electrospray ionization. The identification of the structural motifs and coordination sites within the electrosprayed complexes was achieved by IRMPD spectroscopy and vibrational assignment aided by DFT calculations. The strategy used was based on the gradual increase of the size of the ionic *cis*platin complexes. First the biologically active form of *cis*platin, namely the naked aqua complex *cis*-$[PtCl(NH_3)_2(H_2O)]^+$, was characterized. This key intermediate in *cis*platin chemistry, extensively studied in literature, had never been studied before by means of IRMPD spectroscopy. In solution the aqua complex of *cis*platin (and of *trans*platin) undergoes quickly further hydrolysis reaction and aggregation phenomena which prevent its characterization. The use of ESI-MS has allowed us to identify these reactive intermediates formed in solution, mass-select them as bare ions in the ion trap and interrogate them by the means of the IRMPD. The experimental features have been interpreted by comparison with MP2-calculated linear IR spectra, disclosing the first hydrolytic intermediates of *cis*-and *trans*platin as distinct, non-interconverting species.

Although it is well recognized that *cis*platin interacts with DNA at the N7 position of adenine (A) and guanine (G) nucleobases, the detailed molecular features of the bare complexes between *cis*platin and the nucleobases were not reported. For this reason we decided to investigated the structure of the *cis*-$[PtCl(NH_3)_2(G)]^+$ and *cis*-$[PtCl(NH_3)_2(A)]^+$ complexes obtained by ESI of a solution of *cis*platin with either 2'-deoxyadenosine-5'- monophosphate (5'-dAMP) or 2'-deoxyguanosine-5'-mono- phosphate (5'-dGMP). In agreement with the IR computed spectra of conceivable isomers, IRMPD spectroscopy confirmed that platinum interacts with the N7 position of the guanine in *cis*-$[PtCl(NH_3)_2(G)]^+$. Moreover, the red-shifts of both the carbonyl stretch of the guanine in the fingerprint range and the N-H stretching of the NH_3 ligand of the platinum complex are perfectly consistent with the presence of a strong hydrogen bond between the carbonyl group of the guanine and the hydrogen atom of one ammonia ligand. In contrast, the IRMPD spectra of *cis*-$[PtCl(NH_3)_2(A)]^+$ may be explained with the coexistence of two isomers, where Pt is covalently bonded in the N3 and N1 position of native adenine. By further increasing the complexity of the ligand, we have studied of the interaction of *cis*platin 5'-dGMP, in *cis*-$[Pt(NH_3)_2(5'\text{-dGMP–H})]^+$ and *cis*-$[PtCl(NH_3)_2(5'\text{-dGMP})]^+$ complexes. Moving from the simple nucleobase to the mononucleotide, the number of possible coordinating groups in the complexes obviously increases. In agreement with computational results, the vibrational spectroscopic characterization of the *cis*-$[Pt(NH_3)_2(5'\text{-dGMP–H})]^+$ ion points to a macrochelate species resulting from the simultaneous interaction of the metal with both the N7 atom of the guanine residue and an O atom of the phosphate group, structures that bear features in common with those characterized in solution by NMR spectroscopy. Concerning the *cis*-$[PtCl(NH_3)_2(5'\text{-dGMP})]^+$ ion, our study points to a monodentate complex involving exclusively the N7 position of guanine,

as observed in solution. The IRMPD spectra of the and *cis*-$[PtCl(NH_3)_2(5'\text{-dAMP})]^+$ indicate that hat the sampled ionic population contains two major isomers, with platinum coordinated either to the N3 or to the N1 position of adenosine. IRMPD kinetics have allowed an estimation of their relative proportions. Unexpectedly, the most abundant component of *cis*-$[PtCl(NH_{3)2}(5'\text{-dAMP})]^+$ is the N3 isomer, even if less stable than the other possible isomers. Instead, the presence of calculated global minimum with a metal coordination at the N7 position seems to barely contribute to the sampled ionic population. The interaction of *cis*platin with target amino acids, including L-methionine (Met) and L-histidine (His), has been also addressed. The IRMPD spectra of *cis*-$[PtCl(NH_3)_2(Met)]^+$ has indicated that the *cis*platin attack is mainly directed on the sulfur atom of methionine, while in the corresponding *trans*platin adduct the metal atom can be coordinated either to the sulfur or the nitrogen atom. The comparison between the experimental spectra of the *cis*-$[PtCl(NH_3)_2(His)]^+$ and the calculated ones indicates that the platinum is bound to either the N_π and N_τ imino nitrogen atoms of the imidazole group. Moreover, IRMPD kinetic measurements has allowed us to estimate the individual contributions of N_π and N_τ isomers and conformers based on IRMPD kinetic measurements. A recent application of the combined experimental and theoretical approach has enabled us to reach a comprehensive elucidation at the molecular level of the reactive events responsible for the binding of *cis*platin with (simplified) ligands. To this end, the structure of the apparently five coordinated platinum clusters $[PtCl(NH_3)_2(L)(H_2O)]^+$, obtained by ESI from aqueous solution of *cis*platin with selected ligands L, was investigated by IRMPD and collision induced dissociation (CID) assay. The experimental spectra point to the formation of an encounter complex of the *cis*platin aqua complex solvated by the incoming ligand and represent the first evidence of a prototypical Eigen–Wilkins encounter complex in solution. These results are reported in the following papers: A1, A2, A6, A9, A12, P6 and P7.

(b) Structural and functional consequence of post- translational modifications (PTMs) of amino acids and peptides.

PTMs are recognized to increase the functional diversity of protein by the covalent addition of functional groups. These modifications, which comprise, among others, thiol oxidation, nitrosylation, phosphorylation, glycosylation and sulfation, influence almost all aspects of normal cell activity and pathogenesis. Therefore, detecting and understanding PTMs is a crucial aim in the study of cell biology and disorder healing and prevention. The unambiguous and detailed characterization of the structural and dynamic behavior of the transient intermediates deriving from: i) S-nitrosation, namely S-nitrosocysteine, S-nitroglutathione, a cysteine containing tripetide; ii) 4-hydroxylation, including (2S,4R)-4-hydroxyproline, found in the Y-position of protocollagen chains; iii) O-sulfation, namely serine-O-sulfate; iv) thiol oxidation, including the sulfenic, sulfinic and sulfonic forms of cysteine, has been accomplished by the combined approach in the gas phase, where external interferences are absent. Regarding the cysteine thiol oxidation, we could obtain the structural assignment of the deprotonated cysteine sulfenic, sulfinic and sulfonic acids ions $[cysSO_x]^-$ (where x = 1, 2 and 3 respectively), key and elusive intermediates in the redox-switching chemistry of proteins. In all cases there are two possible deprotonation sites, either the (oxidized) thiol or the carboxylic group. While deprotonated cysteine sulfenic acid is deprotonated fat the carboxylic group, the cysteine sulfonic acid results deprotonated on the sulfonate group. For the sulfinic form, $[cysSO_2]^-$ no correspondence was found between the

experimental and the DFT calculated spectra of both the possible deprotonated forms. This discrepancy was solved with the use of ab initio molecular dynamic calculations showing that $[cysSO_2]^-$ anion can exist in both the deprotonated forms where the proton is almost free to move from one basic site to the other. The results are presented in the following papers: A3, A4, P12, P20, A7, P23, P32, P34,P38 and P40.

(c) Reactivity of iron porphyrin complexes, Fe^{III}-heme$^+$ and Fe^{II}-HemeH$^+$

In these studies, we wanted to highlight the role of the iron oxidation state in naked ferric and ferrous heme ions without additional effects like solvent and axial ligand. While the ferric heme, where the metal is coordinated by the dianion of protoporphyrin IX, Fe^{III}-heme$^+$, is delivered in the gas-phase by direct ESI of a Hemin chloride solution, the ferrous heme complex is overall neutral and therefore not directly amenable to be studied by MS. An alternative procedure based on CID of ESI formed ions of microperoxidase (MP11) solution allowed us to obtain the protonated form of Fe^{II}-Heme. The reactivity of both heme ions was then investigated by FT-ICR MS, IRMPD spectroscopy and theoretical calculations. The observed ion chemistry towards Hydrogen/Deuterium exchange supports very similar features for both Fe^{III}-heme$^+$ and Fe^{II}-HemeH$^+$ ions. The result is consistent with the two propionic acid functionalities on the periphery of the porphyrin ring being involved in the exchange process. These groups are clearly not involved in the protonation of neutral Fe^{II}-heme to form Fe^{II}-HemeH$^+$. However, the reactivity towards ligands additions is found markedly different for Fe^{III}-heme$^+$, and Fe^{II}-hemeH$^+$ ions: Fe^{III}-heme$^+$ reacts more efficiently with hard ligands in paticular. We have observed a linear coordination between the Gibbs free energy for ligand binding to the heme and the gas phase basicity (GB) of the ligands with a remarkable exception: the nitric oxide. NO displays equilibrium constants for the association with both heme ions that are extraordinarily high considering its low GB value. Furthermore, we experimentally observed that Fe^{III}-heme$^+$ and Fe^{II}-hemeH$^+$ behave very similarly in their gas phase reaction with NO, in contrast with what was found in solution where Iron (II) heme proteins and model complexes react with NO remarkably faster than the respective iron (III) species. The vibrational features of both the bare iron-heme complexes with NO, (studied also using ^{15}NO in order to assign the NO stretching vibrations) indicate that nitrosyl iron(III) complexes are characterized by a linear Fe-NO unit. In contrast, the nitrosyl Fe(II) heme complex may be envisioned as approaching a $Fe^{III}NO^-$ resonance structure with significant π^* electron density on the nitrosyl ligand. Others models of nitrosyl Fe^{III} heme complexes have been characterized: $[Fe(TPP)(NO)]^+$ and $[Fe(TPFPP)(NO)]^+$, (where TPP is 5,10,15,20-tetrakis-phenyl-porphyrin dianion and TPFPP is 5,10,15,20-tetrakis-pentafluorophenyl- porphyrin dianion, respectively) pointing to iron center in a singlet state described as $Fe^{II}(NO^+)$. All the results are reported in the following papers: A11, P14, P17, P18, P19, P28, P39, P41, P47, P48, P49, P52, and P56.

(d) Fundamentals ions

(I) Protonated aromatics

The elucidation of intrinsic features like structure, reactivity, and energetics of ions produced by protonation of simple aromatic molecules, including benzene and its monosubstituted derivatives, is of crucial interest in the field of physical and biological chemistry. When the protonation is directed

on the aromatic ring, an arenium ion is obtained, the key intermediate in electrophilic aromatic substitution reactions. In this context, we have studied several protonated aromatic ions. The vibrational signature of gaseous protonated benzene made possible to definitively ascertain the σ-complex structure for the benzenium ion. The IR spectra of protonated toluene point to the prevalence of ortho/para protonated isomers within the sampled gaseous ionic population, thus confirming our previous radiolytic experiments. Conversely, protonated phenylsilane presents the proton only in the ipso position. Also, we have characterized two pairs of representative members of the important benzylium/tropylium family: hydroxysubstituted benzylium /tropylium and methylbenzylium /methyltropylium ions, both pairs appear to be formed by distinct, non-interconverting isomers. The results are reported in papers: P36, P46, P54, P55, P57, P60, P63, P74 and P80

(II) Cation-π interactions

Non-covalent interactions, including hydrogen-bonding, cation-π interactions and van der Waals interactions, play a paramount role in all areas of chemistry and are substantial in molecular recognition mechanisms. We have studied the formation of non-conventional hydrogen bonds between an aromatic ring and either an oxonium or an ammonium group by varying the length of the aliphatic chain (from 1 to 5 units) in gaseous ϖ-phenylalkyloxonium ions and in ϖ-phenylalkylammonium ions, respectively. The distance between the interacting group is correlated with the strength of the bond between them. The higher homologues display a conformation that allows intramolecular hydrogen bond to be formed. In another study, [Benzene, NO]$^+$ ions were formed in the gas phase by means of two routes. The ions obtained by the NO^+ transfer process to neutral benzene inside the FT-ICR cell showed a non-covalent π-complex motif characterized as η6 complexes with the NO placed perpendicularly in the center of the aromatic ring and marginally bend. On the other hand, the ESI of a methanolic solution of nitrosobenzene yields the covalent bonded N-protonated nitrosobenzene. The results are reported in papers: A8, P11, P16, P53, P61 and P62.

(III) Interaction of anions with π-acidic aromatics

We have examined the binding feature of anionic adducts formed between prototypical electron-deficient aromatic systems (such as 1,3,5,-trinitrobenzene and 2,4,-dinitrotoluene) and exemplary anions (OH^-, OCH_3^-, $OC_2H_5^-$, CN^-, F^-,Cl^-, Br, I^- , and deprotonated pyrrolidine, imidazole, acetone (Ac^-) and acetylacetone). The ions were formed by ESI and probed by IRMPD spectroscopy, CID experiments at variable energy and quantum chemical calculations. The so obtained negatively charged complexes display a σ-adduct structure with variable binding motifs from strongly covalent σ-adduct (Meisenheimer complex) to a weakly covalent σ-complex, depending on the anion basicity. The results are reported in papers: P5, P25, P29, P33, P44 and P51.

(IV) Protonated inorganic acids.

We have characterized the structure and thermodynamics of protonated carbonic acid, protonated sulfuric acid and protonated sulfurous acid, elusive species that were never isolated in solution. The results are reported in papers: A5, P42, P45.

(V) Silyl cation.

The β Silyl effect, the stabilizing effect exerted on a carbenium ion by a silyl group in β position, recognized as one of the most important aspect of the organosilicon chemistry, was highlighted by means of radiolytic experiments through the silylation of alkenes and aromatics, and by the IRMPD spectroscopy of protonated allyl trimethylsilane, with the support of theoretical calculations. Papers: A10, P31, P65, P76, P82.

(e) Untargeted analysis of foodstuff

A recent interest of my research regards the application of advanced mass spectrometric techniques, based on high resolution mass spectrometry measurements (HR-MS) performed by ESI FT-ICR MS and CID experiments, for foodstuff characterization. The determination of the metabolic profile of fruit and vegetable specimens represents an increasingly important topic in view of the characterization and quality assurance of PDO (protected designation of origin) species. The acquisition of elemental composition and structural information, besides further checks with reference compounds and specialized databank, have allowed to identify a number of metabolites in red sweet pepper "Cornetto di Pontecorvo" (C. annuum) as report in paper P1.

Expertise

- Expertise in mass spectrometry (MS): ion traps, triple quadrupole, GC-MS, FT-ICR
- Expertise in measurements with free-electron laser systems and table-top laser systems.
- Expertise in other means for studying gas phase ion chemistry, such as radiolytic techniques and kinetics measurements in ion molecule reactions.

Part IX – Summary of Scientific Achievements

Product type	Number	Data Base	Start	End
Papers [international]	82*	Scopus	1995	2018

*One product reported in the data base is an "addition and correction" on JACS 2011, not considered in this number and also for the evaluation of total values reported below

Index	Database	Value	Value without self-citations of the author according to the requirements of the call
Total Impact factor *	ISI Journal Citation Report	322.108	
Average Impact Factor per Product	ISI Journal Citation Report	3.928	
Total Citations	Scopus	1451	1040
Average Citations per Product	Scopus	17.695	12.683
Hirsch (H) index	Scopus	23	17

***Calculated on the basis of the publication year.

Part X– Selected Publications

A1) Chiavarino, B., Crestoni, M.E., Fornarini, S., Scuderi, D., Salpin, J.-Y.
Undervalued N3 Coordination Revealed in the *Cis*platin Complex with 2'-Deoxyadenosine-5' monophosphate by a Combined IRMPD and Theoretical Study
Inorganic Chemistry, (2017) 56 (15), pp. 8793-8801.
DOI: 10.1021/acs.inorgchem.7b00570
IF = 4.857 – cited 1 time - SOURCE: Scopus

A2) Corinti, D., Coletti, C., Re, N., Chiavarino, B., Crestoni, M.E., Fornarini, S.
*Cis*platin Binding to Biological Ligands Revealed at the Encounter Complex Level by IR Action Spectroscopy
Chemistry - A European Journal, (2016) 22 (11), pp. 3794-3803.
DOI: 10.1002/chem.201504521
IF = 5.317 – cited 14 times - SOURCE: Scopus

A3) Scuderi, D., Bodo, E., Chiavarino, B., Fornarini, S., Crestoni, M.E.
Amino Acid Oxidation: A Combined Study of Cysteine Oxo Forms by IRMPD Spectroscopy and Simulations
Chemistry - A European Journal, (2016), 22 (48), pp. 17239-17250. DOI: 10.1002/chem.201603298
IF = 5.317 – cited 4 times - SOURCE: Scopus

A4) Paciotti, R., Coletti, C., Re, N., Scuderi, D., Chiavarino, B., Fornarini, S., Crestoni, M.E.
Serine O-sulfation probed by IRMPD spectroscopy
Physical Chemistry Chemical Physics, (2015), 17 (39), pp. 25891-25904.
DOI: 10.1039/c5cp01409c
IF = 4.449 – cited 16 times - SOURCE: Scopus

A5) Sinha, R.K., Scuderi, D., Maitre, P., Chiavarino, B., Crestoni, M.E., Fornarini, S.
Elusive sulfurous acid: Gas-phase basicity and IR signature of the protonated species
(2015) Journal of Physical Chemistry Letters, 6 (9), pp. 1605-1610.
DOI: 10.1021/acs.jpclett.5b00450
IF = 8.539 – cited 8 times - SOURCE: Scopus

A6) Chiavarino, B., Crestoni, M.E., Fornarini, S., Scuderi, D., Salpin, J.-Y.

Interaction of *cis*platin with 5'-dgmp: A combined irmpd and theoretical study
(2015) Inorganic Chemistry, 54 (7), pp. 3513-3522.
DOI: 10.1021/acs.inorgchem.5b00070
IF = 4.857 – cited 20 times - SOURCE: Scopus

A7) Lanucara, F., Chiavarino, B., Scuderi, D., Maitre, P., Fornarini, S., Crestoni, M.E.
Kinetic control in the CID-induced elimination of H_3PO_4 from phosphorylated serine probed using IRMPD spectroscopy
(2014) Chemical Communications, 50 (29), pp. 3845-3848.
DOI: 10.1039/c4cc00877d
IF = 6.834 – cited 17 times - SOURCE: Scopus

A8) Chiavarino, B., Crestoni, M.E., Schütz, M., Bouchet, A., Piccirillo, S., Steinmetz, V., Dopfer, O., Fornarini, S.
Cation-π Interactions in Protonated Phenylalkylamines
(2014) Journal of Physical Chemistry A, 118 (34), pp. 7130-7138.
DOI: 10.1021/jp505037n
IF = 2.693 – cited 21 times - SOURCE: Scopus

A9) De Petris, A., Ciavardini, A., Coletti, C., Re, N., Chiavarino, B., Crestoni, M.E., Fornarini, S.
Vibrational signatures of the naked aqua complexes from platinum(II) anticancer drugs
(2013) Journal of Physical Chemistry Letters, 4 (21), pp. 3631-3635.
DOI: 10.1021/jz401959s
IF = 6.687 – cited 26 times - SOURCE: Scopus

A10) Chiavarino, B., Crestoni, M.E., Lemaire, J., Maitre, P., Fornarini, S.
Communication: Infrared spectroscopy of protonated allyl-trimethylsilane: Evidence for the β-silyl effect
(2013) Journal of Chemical Physics, 139 (7), art. no. 071102
DOI: 10.1063/1.4818729
IF = 3.122 – cited 2 times - SOURCE: Scopus

A11) Lanucara, F., Scuderi, D., Chiavarino, B., Fornarini, S., Maitre, P., Crestoni, M.E.
IR signature of NO binding to a ferrous heme center
(2013) Journal of Physical Chemistry Letters, 4 (15), pp. 2414-2417.
DOI: 10.1021/jz401141p
IF = 6.687 – cited 20 times - SOURCE: Scopus

A12) Chiavarino, B., Crestoni, M.E., Fornarini, S., Scuderi, D., Salpin, J.-Y.
Interaction of *cis*platin with adenine and guanine: A combined IRMPD, MS/MS, and theoretical study
(2013) Journal of the American Chemical Society, 135 (4), pp. 1445-1455.
DOI: 10.1021/ja309857d
IF = 11.444 – cited 38 times - SOURCE: Scopus

Roma, 4 luglio 2018

Barbara Chiavarino